24/09/200410700019

FULL SCREEN SEARCH COMPLETED - 1307 TO ITERATE

100.0% PROCESSED 1307 ITERATIONS 16 ANSWERS
SEARCH TIME: 00.00.01

L2 16 SEA SSS FUL L1

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.42	155.63

FILE 'CAPLUS' ENTERED AT 10:44:23 ON 24 SEP 2004
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FILE COVERS 1907 - 24 Sep 2004 VOL 141 ISS 14
FILE LAST UPDATED: 23 Sep 2004 (20040923/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L3 103 L2

=> d ibib abs hitstr 1-30

L3 ANSWER 1 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:589414 CAPLUS
DOCUMENT NUMBER: 141:134107
TITLE: A method for the treatment, prevention, or inhibition of a CNS disorder and/or pain and inflammation using a combination of duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor and compositions thereof
INVENTOR(S): Arneric, Stephen P.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060366	A1	20040722	WO 2003-US38751	20031206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

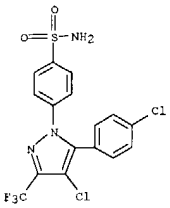
PRIORITY APPLN. INFO.: US 2002-433790P P 20021217

AB A method of treating, preventing, or inhibiting a CNS disorder and/or pain and inflammation or an inflammation-associated disorder in a subject in need of such treatment or prevention provides for treating the subject with duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor or prodrug thereof, wherein the amount of duloxetine, venlafaxine or atomoxetine and the amount of a cyclooxygenase-2 selective inhibitor or prodrug thereof together constitute a CNS disorder, pain and inflammation, or inflammation-associated disorder suppressing treatment, prevention, or inhibition effective amount of the composition Compns. and pharmaceutical compns. that contain duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor are also disclosed.

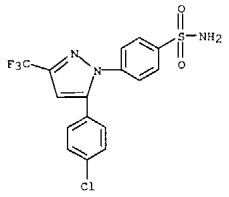
IT **170569-50-3 170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treatment, prevention, or inhibition of CNS disorder and/or

L3 ANSWER 1 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
pain and inflammation using combination of duloxetine, venlafaxine or atomoxetine and cyclooxygenase-2 inhibitor)

RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 2 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:353144 CAPLUS
DOCUMENT NUMBER: 140:368700
TITLE: Methods using exemestane, alone or with other therapeutic agents, for treating estrogen-dependent disorders
INVENTOR(S): Wajszczuk, Charles Paul; Gans, Hendrik J. Dekoning; Di Salle, Enrico; Piscitelli, Gabriella; Massimini, Giorgio; Purandare, Dinesh
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of WO 2002 72,106.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004082557	A1	20040429	US 2003-611653	20030702
WO 2002072106	A2	20020919	WO 2002-EP638	20020118
WO 2002072106	A3	20031030		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

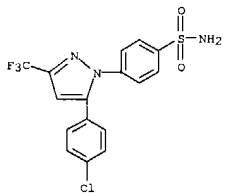
PRIORITY APPLN. INFO.: US 2001-770911 B2 20010126
WO 2002-EP638 A2 20020118
US 2002-393320P P 20020702

AB The invention discloses a method of preventing and/or treating estrogen-dependent disorders selected from endometriosis, uterine fibroids, dysfunctional uterine bleeding, endometrial hyperplasia, polycystic ovarian disease, fibrocystic breast disease and fibrocystic mastopathy, which comprises administering to a female mammal in need of such treatment an effective amount of aromatase inactivator exemestane, alone or in combination with addnl. therapeutic agents. The invention also discloses a method for treating infertility in a female mammal in need of the infertility treatment, comprising administering an effective amount of exemestane to the mammal.

IT **170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exemestane, alone or with other therapeutic agents, for treating estrogen-dependent disorders)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

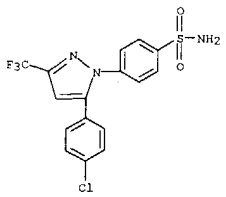
L3 ANSWER 2 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L3 ANSWER 3 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:298293 CAPLUS
DOCUMENT NUMBER: 140:387932
TITLE: Cyclooxygenase (COX)-2-dependent effects of the inhibitor SC236 when combined with ionizing radiation in mammary tumor cells derived from HER-2/neu mice
AUTHOR(S): Lanza-Jacoby, Susan; Dicker, Adam P.; Miller, Sheldon; Rosato, Francis E.; Flynn, John T.; Lavorgna, Stephanie N.; Burd, Randy
CORPORATE SOURCE: Jefferson Medical College, Departments of Surgery, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SOURCE: Molecular Cancer Therapeutics (2004), 3(4), 417-424
CODEN: MCTOCF; ISSN: 1535-7163
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclooxygenase (COX)-2-derived prostaglandins (PGs) are thought to contribute to tumor growth and resistance to radiation therapy. COX-2 protein expression is increased in many tumors including those of the breast. COX-2-derived PGs have been shown to protect cells from radiation damage. This study evaluated the role of COX-2-derived PG in radiation treatment by using the NMF11.2 mammary tumor cell line originally obtained from HER-2/neu mice that overexpress HER-2/neu. We determined whether the effects of the COX-2 inhibitor SC236 on cell growth, radiation-induced PGE2 production and COX expression, cell cycle redistribution, and vascular endothelial growth factor (VEGF) were acting through COX-2-dependent mechanisms. The NMF11.2 cells expressed both COX-1 and COX-2 protein and mRNA. The radiation treatment alone led to a dose-dependent increase in the levels of COX-2 mRNA and COX-2 protein, which was associated with an increase in the production of PGE2 and prostacyclin (PGI2). Treating NMF11.2 cells with high concns. (20 μM) of SC236 for 48 h reduced the radiation-induced increase in COX-2 activity and also decreased cell growth. SC236 (20 μM) increased the accumulation of the cells in the radiosensitive G2-M phase of the cell cycle. However, a low concentration (5 μM) of SC236 was adequate to reduce COX-2 activity. The lower concentration of SC236 (5 μM) also decreased cell growth after a longer incubation period (96 h) and, in combination with a 2 or 5 Gy dose, led to an accumulation of cells in G2-M phase. Restoring PG to control values in cells treated with 5 μM SC236 prevented the growth inhibition and G2-M cell cycle arrest. Radiation treatment of NMF11.2 cells also increased VEGF protein expression and VEGF secretion in a dose-dependent manner, which was blocked in those cells pretreated with 20 μM SC236 but not in those pretreated with 5 μM SC236. These findings indicate that the COX-2 inhibitor SC236 reduced cell growth and arrested cells in the G2-M phase of the cell cycle by mechanisms that are both dependent and independent of PG production while its effects on VEGF appear to be independent of COX-2.

L3 ANSWER 3 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **170569-86-5**, SC236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase (COX)-2-dependent effects of the inhibitor SC236 when combined with ionizing radiation in mammary tumor cells derived from HER-2/neu mice)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

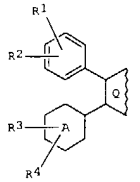


REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:246964 CAPLUS
DOCUMENT NUMBER: 140:287382
TITLE: A preparation of (hetero)cyclic calcium-activated potassium channel activators useful for treatment of, e.g., pollakiuria and urinary
INVENTOR(S): Kono, Rikako; Kohnomi, Shuntarou; Aihara, Hajime; Hosaka, Toshihiro; Kashiwagi, Toshihiko
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1400243	A1	20040324	EP 2003-255860	20030918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			JP 2002-272662	A 20020919
			JP 2003-70298	A 20030314
			JP 2003-278699	A 20030724

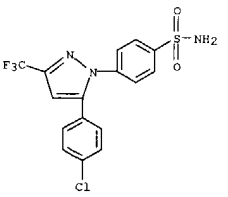
OTHER SOURCE(S): MARPAT 140:287382
GI



I

AB The invention relates to a preparation of (hetero)cyclic compds. of formula I [wherein: A = benzene, pyridine, cycloalkane; Q = (un)substituted imidazole, oxazole, cyclopentane, pyrrole, or pyridine, etc.; R1 = halogen, aminosulfonyl, alkylsulfonyl, alkanoylaminosulfonyl; R2 = H or halogen; R3, R4 = H, halogen, alkyl, alkoxy; rings A and Q may be fused to each other], useful as large-conductance calcium-activated potassium channel openers. Compds. I have excellent large conductance Ca-activated K-channel opening activity, and are useful for the treatment of hypertension, premature birth, pollakiuria, and urinary incontinence, etc. Compds. I (prepns. referenced, phys. data for 27 compds.) were tested for a relaxation effect on potassium-induced contraction of isolated rabbit urinary bladder and inhibitory effect on the rhythmic bladder contractions induced by substance P in anesthetized rats.

L3 ANSWER 4 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **170569-86-5P**, 4-[5-(4-Chlorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]benzenesulfonamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (hetero)cyclic compds. useful as calcium-activated potassium channel openers/activators)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

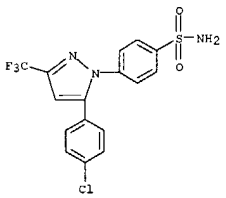
L3 ANSWER 5 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:182705 CAPLUS
DOCUMENT NUMBER: 140:193119
TITLE: Multifunctional COX-2 inhibitors for therapy of cancer, Alzheimer's disease and atherosclerosis
INVENTOR(S): Dannenberg, Andrew J.; Subbaramaiah, Kotha
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017967	A1	20040304	WO 2003-US19549	20030709
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2002-404911P P 20020822

AB Selective inhibitors of cyclooxygenase-2 (COX-2) and selective inhibitors of COX-1 are screened for COX protein independent therapeutic activity. Selective inhibitors of COX-2 and COX-1 are screened for at least two of (a) activation of peroxisome proliferator response element (PPRE) luciferase by at least 100%, (b) at least 50% decrease in level of or 50% downregulation of expression of Class I family of receptors tyrosine kinase, (c) at least 50% downregulation of expression of cyclin D1, (d) at least 50% downregulation of expression of HPV16 oncoproteins E6 and E7, (e) at least 50% increase in expression of PTEN, (f) at least 50% inhibition of tcf/lef/β-catenin-mediated promoter activation, and (g) at least 50% increase in level of Nrf-2. Compds. passing screening testing are indicated for treatment of those having or at risk for cancer, Alzheimer's disease and atherosclerosis. For example, SC-560 caused dose dependent activation of PPRE luciferase and activated PPRE luciferase by more than 100% at concns. tested. Also, a rate of progression of colon cancer in a male patient decreased after the patient was given and maintained on celecoxib or SC-236, 800 mg twice daily.

IT **170569-86-5**, SC-236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(screening of multifunctional COX-2 and COX-1 inhibitors for treatment of Alzheimer's disease, atherosclerosis and cancer)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:182531 CAPLUS
DOCUMENT NUMBER: 140:229475
TITLE: Combinations of ω-3 fatty acids and cyclooxygenase-2 inhibitors for the treatment or prevention of cardiovascular disease, inflammation-related conditions, and cancer
INVENTOR(S): Obukowicz, Mark G.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 49 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

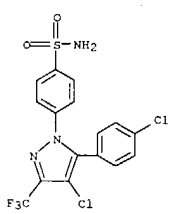
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004044028	A1	20040304	US 2002-113269	20020401

PRIORITY APPLN. INFO.: US 2001-280183P P 20010330

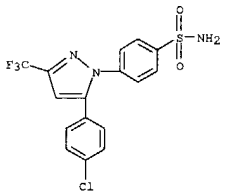
OTHER SOURCE(S): MARPAT 140:229475

AB The invention discloses combinations of ω-3 polyunsatd. fatty acids (PUFAs) and cyclooxygenase-2 selective inhibitors for treatment or prevention of cardiovascular disease, inflammation-related disorders or cancer. The preferred ω-3 PUFAs of the invention have 18-22 carbon atoms, and more preferably 20-22 carbon atoms.

IT **170569-50-3 170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of ω-3 fatty acids and cyclooxygenase-2 inhibitors for treatment or prevention of cardiovascular disease, inflammation-related conditions, and cancer)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 7 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:142952 CAPLUS
DOCUMENT NUMBER: 140:175165
TITLE: Amyloid immunization and COX-2 inhibitors for the treatment of Alzheimer's disease
INVENTOR(S): Robertson, David W.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014367	A2	20040219	WO 2003-US24263	20030804
WO 2004014367	A3	20040325		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
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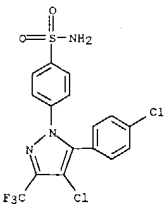
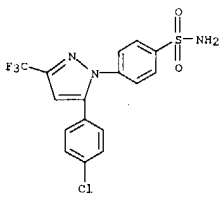
US 2004138296	A1	20040715	US 2003-627357	20030725
PRIORITY APPLN. INFO.:			US 2002-402655P	P 20020812
			US 2002-402674P	P 20020812
			US 2002-402675P	P 20020812
			US 2002-402676P	P 20020812
			US 2002-402760P	P 20020812
			US 2002-402773P	P 20020812
			US 2002-402778P	P 20020812

OTHER SOURCE(S): MARPAT 140:175165
AB The invention provides compns. and methods for the treatment or prevention of Alzheimer's disease. More particularly, the invention provides a combination therapy for the treatment or prevention of Alzheimer's disease, wherein the therapy comprises administering to a subject an amyloid-β vaccine in combination with a cyclooxygenase-2 selective inhibitor.
IT **170569-50-3 170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amyloid immunization and COX-2 inhibitors for treatment of Alzheimer's

L3 ANSWER 7 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
disease)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

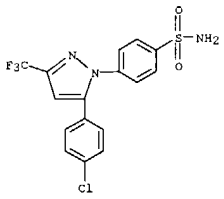


RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 8 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:115468 CAPLUS
DOCUMENT NUMBER: 141:150544
TITLE: Cyclooxygenase-2 inhibitor (SC-236) suppresses activator protein-1 through c-Jun NH2-terminal kinase
AUTHOR(S): Wong, Benjamin Chun-Yu; Jiang, Xiao Hua; Lin, Marie C.
M.; Tu, Shui Ping; Cui, Jian Tao; Jiang, Shi Hu; Wong,
Wai Man; Yuen, Man Fung; Lam, Shiu Kum; Kung, Hsiang Fu
CORPORATE SOURCE: Department of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong, Hong Kong
SOURCE: Gastroenterology (2004), 126(1), 136-147
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background & Aims: Aspirin exerts antitumor effect partly through blocking tumor promoter-induced activator protein-1 (AP-1) activation. The aim of this study is to determine how specific COX-2 inhibitor SC-236 mediates antitumor effect by modulation of AP-1-signaling pathway. Methods: AP-1 transcriptional activity and DNA-binding activity were detected by luciferase reporter assay and gel shift assay, sep. Mitogen-activated protein kinase (MAPK) activation was determined by Western blot and in vitro kinase assay. Antisense oligonucleotide against c-Jun-N-terminal kinase (JNK) was used to suppress JNK expression. Results: We showed that SC-236 inhibited 12-O-tetradecanoylphorbol-13-acetate (PMA)-induced cell transformation in a dose-dependent manner in JB6 cells. At a dose range (12.5-50 μmol/L) that inhibited cell transformation, SC-236 also inhibited anchorage-independent cell growth and AP-1-activation in 3 gastric cancer cells, independent of COX-prostaglandin synthesis. SC-236 down-regulated c-Jun-NH2-terminal kinase phosphorylation and activity. Suppression of JNK activity reversed the inhibitory effect on AP-1 activity by SC-236 and suppressed gastric cancer cell growth, indicating that the inhibitory effect of SC-236 on AP-1 activation and cell growth was through interaction with JNK. Conclusions: The inhibitory effect on JNK-c-Jun/AP-1 activation contributes to the antitumor effect of COX-2-specific inhibitor, and inhibition of JNK activation may have a therapeutic benefit against gastric cancer.
IT **170569-86-5**, SC-236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SC-236 inhibit PMA-induced cell transformation in mouse JB6 cells, inhibited anchorage-independent cell growth, AP-1 activation dose-dependently, down-regulated JNK phosphorylation in human gastric cancer cells)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 8 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



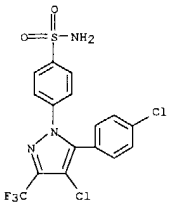
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:41336 CAPLUS
DOCUMENT NUMBER: 140:105282
TITLE: Cyclooxygenase-2 inhibitors and thrombolytic agents for the treatment or prevention of a vaso-occlusive event
INVENTOR(S): Isaksen, Peter C.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

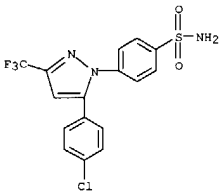
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004833	A1	20040115	WO 2003-US20558	20030630
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004063697	A1	20040401	US 2003-610085	20030630
PRIORITY APPLN. INFO.:			US 2002-393136P P	20020702
			US 2002-393172P P	20020702
			US 2002-393199P P	20020702
			US 2002-393258P P	20020702
			US 2002-393269P P	20020702
			US 2002-393296P P	20020702
			US 2002-393297P P	20020702

AB The present invention provides compns. and methods for the treatment or prevention of a vaso-occlusive event. More particularly, the invention provides a combination therapy for the treatment or prevention of a vaso-occlusive event comprising the administration to a subject of a thrombolytic agent in combination with a cyclooxygenase-2 selective inhibitor. Thrombosis was induced in mice, and the above combination therapy was administered to the mice to treat a vaso-occlusive event.
IT **170569-50-3 170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors and thrombolytic agents for treatment of vaso-occlusive event)

L3 ANSWER 9 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

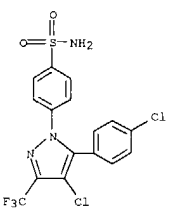


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1007863 CAPLUS
DOCUMENT NUMBER: 140:35975
TITLE: Compositions of tricyclic cyclooxygenase-2 selective inhibitors and acetaminophen for treatment and prevention of inflammation, inflammation-mediated disorders and pain
INVENTOR(S): Seibert, Karen
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 82 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

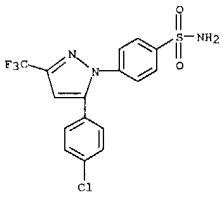
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003236293	A1	20031225	US 2002-246848	20020918
PRIORITY APPLN. INFO.:			US 2001-322932P P	20010918

OTHER SOURCE(S): MARPAT 140:35975
AB A composition is provided comprising a tricyclic cyclooxygenase-2 selective inhibitor and acetaminophen. The composition is effective for the treatment and prevention of inflammation, an inflammation-mediated disorder, and pain. A method of treatment is also claimed wherein the therapeutic effect is through prostaglandin synthesis inhibition.
IT **170569-50-3 170569-86-5**, 4-[5-(4-Chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of tricyclic cyclooxygenase-2 selective inhibitors and acetaminophen for treatment and prevention of inflammation, inflammation-mediated disorders and pain)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

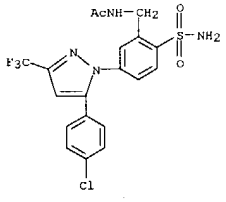


RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, [illegible]methyl)-1H-pyrazol-1-

L3 ANSWER 10 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
yl]- (9CI) (CA INDEX NAME)

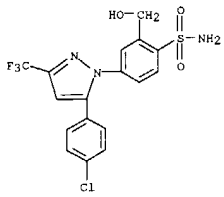


L3 ANSWER 11 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1001998 CAPLUS
DOCUMENT NUMBER: 140:314411
TITLE: Polar substitutions in the benzenesulfonamide ring of celecoxib afford a potent 1,5-diarylpyrazole class of COX-2 inhibitors
AUTHOR(S): Singh, Sunil K.; Reddy, P. Ganapati; Rao, K. Srinivasa; Lohray, Braj B.; Misra, P.; Rajjak, Shaikh A.; Rao, Yeleswarapu K.; Venkateswarlu, A.
CORPORATE SOURCE: Discovery Chemistry, Discovery Research-Dr. Reddy's Laboratories Ltd, Miyapur, Hyderabad, 500 049, India
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(2), 499-504
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several chemical modifications in the N1-benzenesulfonamide ring of celecoxib
are presented. The series with a hydroxymethyl group adjacent to the sulfonamide was found to be the most potent modification that yielded many
compds. selectively active against COX-2 enzyme in vitro.
IT **678987-48-9P 678987-58-1P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polar substitutions in benzenesulfonamide ring of celecoxib afford a potent 1,5-diarylpyrazole class of COX-2 inhibitors)
RN 678987-48-9 CAPLUS
CN Acetamide,
N-[[2-(aminosulfonyl)-5-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 678987-58-1 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-2-(hydroxymethyl)- (9CI) (CA INDEX NAME)

L3 ANSWER 11 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



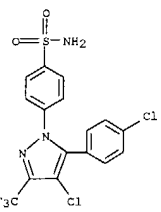
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 12 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:971878 CAPLUS
DOCUMENT NUMBER: 140:13075
TITLE: Monotherapy for the treatment of amyotrophic lateral sclerosis with cyclooxygenase-2 (COX 2) inhibitor(s)
INVENTOR(S): Isakson, Peter C.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

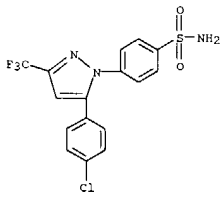
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101441	A1	20031211	WO 2003-US14548	20030528
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004063752	A1	20040401	US 2003-444072	20030523
PRIORITY APPLN. INFO.:			US 2002-384139P P	20020531
			US 2003-444072 A	20030523

OTHER SOURCE(S): MARPAT 140:13075
AB A method of treating, preventing, or inhibiting amyotrophic lateral sclerosis (ALS), in a subject in need of such treatment, inhibition or prevention. The method comprises administering to a subject one or more cyclooxygenase-2 selective inhibitor(s), or isomer(s), or pharmaceutically
acceptable salt(s), ester(s), or prodrug(s) thereof, wherein the amount of
the cyclooxygenase-2 selective inhibitor(s), isomer(s), ester(s), salt(s) or prodrug(s) thereof constitutes an ALS treatment, inhibition or prevention effective amount of the COX 2 inhibitor(s).
IT **170569-50-3 170569-86-5**, 4-[5-(4-Chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monotherapy for treatment of amyotrophic lateral sclerosis with selective cyclooxygenase-2 inhibitor(s) over cyclooxygenase-1)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide,
4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 12 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



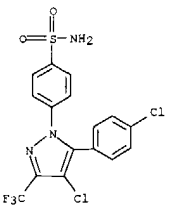
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 13 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:971836 CAPLUS
DOCUMENT NUMBER: 140:23256
TITLE: Combination therapy for treatment of amyotrophic lateral sclerosis (ALS) with cyclooxygenase-2 (COX 2) inhibitor(s) and a second drug
INVENTOR(S): Isakson, Peter C.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 358 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

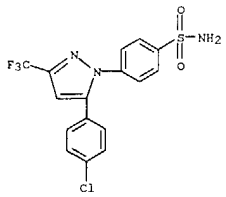
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101380	A2	20031211	WO 2003-US14547	20030528
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004063751	A1	20040401	US 2003-444071	20030523
PRIORITY APPLN. INFO.:			US 2002-384104P	P 20020531
			US 2003-444071	A 20030523

OTHER SOURCE(S): MARPAT 140:23256
AB A method of treating, preventing, or inhibiting ALS, in a subject in need of such treatment, inhibition or prevention. The method comprises administering to a subject one or more cyclooxygenase-2 selective inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof, in combination with one or more second drugs, wherein the amount of the cyclooxygenase-2 selective inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof in combination with the amount of second drug(s) constitutes an ALS treatment, inhibition or prevention effective amount
IT **170569-50-3 170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for amyotrophic lateral sclerosis treatment of with COX-2 inhibitor and second drug)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 13 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



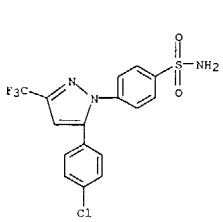
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 14 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:950052 CAPLUS
DOCUMENT NUMBER: 140:13040
TITLE: Combined use of TACE inhibitors and COX2 inhibitors as anti-inflammatory agents
INVENTOR(S): Duan, Jingwu
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003225054	A1	20031204	US 2003-453036	20030603
PRIORITY APPLN. INFO.:			US 2002-385656P	P 20020603

OTHER SOURCE(S): MARPAT 140:13040
AB This invention relates to a method of treating inflammatory diseases in a mammal comprising administering to the mammal a therapeutically effective amount of a combination of: (i) at least one TACE inhibitor, (ii) one or more anti-inflammatory agents selected from the group consisting of: selective COX-2 inhibitors, interleukin-1 antagonists, dihydroorotate synthase inhibitors, p38 MAP kinase inhibitors, TNF-α inhibitors, TNF-α sequestration agents, and methotrexate. The invention also relates to compns. and kits containing the same.
IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined use of TACE inhibitors and COX2 inhibitors as anti-inflammatory agents)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

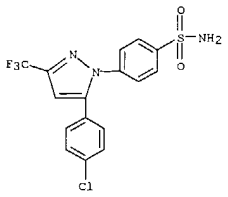


L3 ANSWER 15 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:931110 CAPLUS
DOCUMENT NUMBER: 139:391352
TITLE: Methods and compositions for treating T cell mediated inflammatory/autoimmune diseases and disorders in subjects having a glucocorticoid regulation deficiency
INVENTOR(S): Brewer, Judson A.; Muglia, Louis J.
PATENT ASSIGNEE(S): The Washington University, USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003096970	A2	20031127	WO 2003-US13548	20030501
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004027789	A1	20040205	US 2003-427683	20030501
PRIORITY APPLN. INFO.:			US 2002-377112P	P 20020502
			US 2002-381188P	P 20020516

AB The present invention provides a method for preventing or treating a T cell mediated inflammatory/autoimmune disease or disorder in a subject having a glucocorticoid regulation deficiency, where the method comprises administering to a subject in need of such treatment a cyclooxygenase-2 inhibitor. The Cox-2 inhibitor may be administered in combination with a glucocorticoid. The Cox-2 inhibitor can be a Cox-2 selective inhibitor. Compns., pharmaceutical compns. and kits are provided for carrying out the method.
IT **170569-86-5**, SC236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of T cell mediated inflammatory/autoimmune diseases and disorders in subjects having a glucocorticoid regulation deficiency using cyclooxygenase 2 inhibitor combined with glucocorticoid)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 15 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



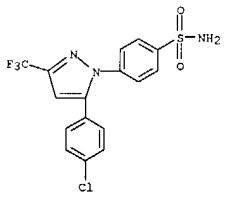
L3 ANSWER 16 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:871671 CAPLUS
DOCUMENT NUMBER: 141:99471
TITLE: Neurones treated with cyclo-oxygenase-1 inhibitors are resistant to amyloid-β1-42
AUTHOR(S): Bate, Clive; Veerhuis, Robert; Eikelenboom, Piet; Williams, Alun
CORPORATE SOURCE: Institute of Comparative Medicine, Depart of Veterinary Pathology, Glasgow University Veterinary School, Glasglow, G61 1QH, UK
SOURCE: NeuroReport (2003), 14(16), 2099-2103
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB SUMMARY: Epidemiol. studies have shown that the risk of developing Alzheimer's disease is reduced by the chronic use of classical non-steroidal anti-inflammatory drugs (NSAIDs), drugs that inhibit the cyclo-oxygenase (COX) enzymes that convert arachidonic acid to prostaglandins. In the present study, human SH-SY5Y neuroblastoma cells or murine primary cortical neurons treated with NSAIDs were protected against the otherwise toxic effects of amyloid-β1-42. COX-1 selective inhibitors provided greater protection than did COX-2 selective inhibitors or lipoxygenase inhibitors, suggesting that activation of COX-1 is required for amyloid-β1-42-induced neurotoxicity. Although the production of neuronal prostaglandin E2 in response to amyloid-β1-42 was reduced by the presence of COX-1 inhibitors, no neurotoxic effects of prostaglandin E2, or any other prostaglandin, were observed

IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of COX-1, COX-2 and lipoxygenase selective inhibitors on amyloid-β1-42 induced neurotoxicity in human and murine cells)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 16 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:855795 CAPLUS
DOCUMENT NUMBER: 139:345939
TITLE: Monotherapy for the treatment of Parkinson's disease with cyclooxygenase 2 (COX2) inhibitor(s)
INVENTOR(S): Stephenson, Diane T.; Isakson, Peter C.; Maziasz, Timothy J.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 186 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003088959	A2	20031030	WO 2003-US11517	20030414
WO 2003088959	A3	20031231		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004006100	A1	20040108	US 2003-412970	20030414
PRIORITY APPLN. INFO.:			US 2002-373317P	P 20020418

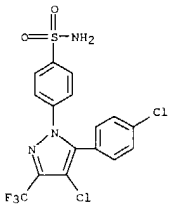
OTHER SOURCE(S): MARPAT 139:345939

AB The invention provides a method for treating, preventing, or inhibiting Parkinson's disease (PD), in a subject in need of such treatment, inhibition or prevention. The method comprises treating the subject with one or more COX2 selective inhibitor(s), ester(s), salt(s) or prodrug(s) thereof, wherein the amount of the cyclooxygenase-2 selective inhibitor(s), ester(s), salt(s) or prodrug(s) thereof constitutes a PD treatment-, inhibition- or prevention-effective amount of the COX2 inhibitor(s).

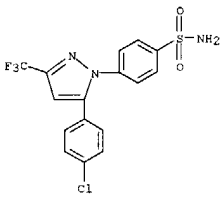
IT **170569-50-3 170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 (COX2) inhibitor for treatment of Parkinson's disease)

RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 17 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

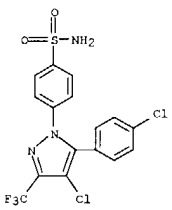


L3 ANSWER 18 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:855794 CAPLUS
DOCUMENT NUMBER: 139:345938
TITLE: Combination therapy including cyclooxygenase 2 (COX2) inhibitor(s) for the treatment of Parkinson's disease
INVENTOR(S): Stephenson, Diane T.; Isakson, Peter C.; Maziasz, Timothy J.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 266 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

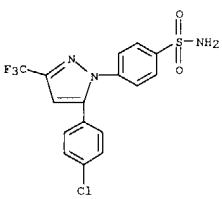
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003088958	A2	20031030	WO 2003-US11269	20030414
WO 2003088958	A3	20040819		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004034083	A1	20040219	US 2003-413348	20030414
PRIORITY APPLN. INFO.:			US 2002-373311P P	20020418

OTHER SOURCE(S): MARPAT 139:345938
AB The invention discloses a method for treating, preventing, or inhibiting Parkinson's disease (PD) in a subject in need of such treatment, inhibition, or prevention. The method comprises treating the subject with one or more COX2 selective inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof, in combination with one or more second drugs, wherein the amount of the COX2 selective inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof in combination with the amount of second drug(s) constitutes a PD treatment-, inhibition- or prevention-effective amount
IT **170569-50-3 170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy including cyclooxygenase 2 inhibitor for treatment of Parkinson's disease)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide,
4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 18 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



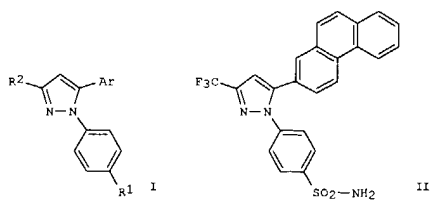
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 19 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:836766 CAPLUS
DOCUMENT NUMBER: 139:350731
TITLE: Preparation of 1-phenyl-1H-pyrazoles for inducing apoptosis in proliferating cells
INVENTOR(S): Chen, Ching-shin; Song, Xueqin; Lin, Ho-pi
PATENT ASSIGNEE(S): The Ohio State University Research Foundation, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

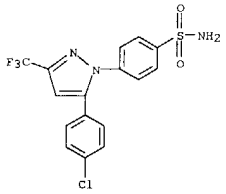
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086287	A2	20031023	WO 2003-US10738	20030408
WO 2003086287	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003236294	A1	20031225	US 2003-409502	20030408
PRIORITY APPLN. INFO.:			US 2002-370664P P	20020408

OTHER SOURCE(S): MARPAT 139:350731
GI



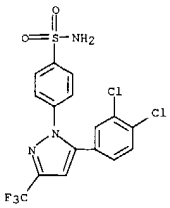
AB Title compds. I [wherein R1 = carboxamido; R2 = (halo)alkyl; Ar = (un)substituted Ph biphenyl, naphthyl, anthryl, phenanthrenyl, or fluorenyl; and pharmaceutically acceptable salts thereof] were prepared and tested for their effects on cyclooxygenase-2 (COX-2) activity, the

L3 ANSWER 19 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
viability of human prostate cancer PC-3 cells, and their ability to induce
apoptosis in these cells. For example, Claisen condensation of 2-acetylphenanthrene with Et trifluoroacetate in the presence of NaH afforded the 1,3-keto-enol deriv. (95%). Reaction with (4-sulfamoylphenyl)hydrazine•HCl in EtOH gave 4-[5-(2-phenanthrenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide (II) in 65% yield. A
structure-activity anal. of derivs. of the COX-2 inhibitor celecoxib found
no correlation between the COX-2 inhibitory and apoptosis-inducing activities. For instance, increased polarity or bulkiness of the terminal
Ph ring reduced the ability of compds. to inhibit COX-2, while a certain degree of bulkiness and hydrophobicity in the substituted Ph ring was highly desirable for apoptosis induction in PC-3 cells. Thus, I are useful for inducing apoptosis in proliferating cells, particularly cancer cells, including but not limited to prostate cancer, leukemia, non-small cell lung cancer, colon cancer, CNS cancer, melanoma, ovarian cancer, renal cancer, bladder cancer, lymphoma, and breast cancer. These compds. are particularly useful in the treatment of androgen-independent cancers, including hormone-refractory prostate cancer.
IT **170569-86-5P**, 4-[5-(4-Chlorophenyl)-3-trifluoromethyl-1H-pyrazol-1-yl]benzenesulfonamide **170569-92-3P 170569-94-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiproliferative agent; preparation of 1-Ph-1H-pyrazoles for inducing
apoptosis in proliferating cells)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

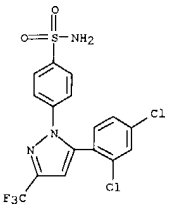


RN 170569-92-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 19 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

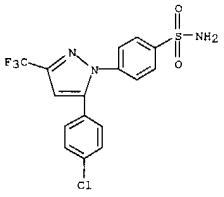


RN 170569-94-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 20 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:813608 CAPLUS
DOCUMENT NUMBER: 140:331916
TITLE: Cox-2 is needed but not sufficient for apoptosis induced by Cox-2 selective inhibitors in colon cancer cells
AUTHOR(S): Agarwal, B.; Swaroop, P.; Protiva, P.; Raj, S. V.; Shirin, H.; Holt, P. R.
CORPORATE SOURCE: School of Medicine, Division of Gastroenterology, St. Louis University, St. Louis, MO, 63105, USA
SOURCE: Apoptosis (2003), 8(6), 649-654
CODEN: APOPFN; ISSN: 1360-8185
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of Cox-2 in NSAID-induced apoptosis is debated. We studied the role of Cox-2 inhibition in apoptosis induced by a selective Cox-2 inhibitor, SC 236 (a structural analog of celecoxib) in two colon cancer cell lines, HT29 (expressing Cox-2 protein) and HCT116 (not expressing Cox-2 protein). Apoptosis was quantified by flow cytometry. SC 236 0-75 μM decreased cell nos. and induced apoptosis to identical levels in HT29 and HCT116 cells. However, SC 236, concns. >75 μM reduced Cox-2 protein expression in HT29 cells and induced greater levels of apoptosis in HT29 than in HCT116 cells. In contrast, sulindac sulfide (SSD) (which inhibits Cox-1 and Cox-2) 0-200 μM or sulindac sulfone (SSN) 0-500 μM (without significant activity against Cox-1 or Cox-2) caused identical decreases in cell number and increases in apoptosis in HT29 and HCT116 cells. Neither SSD nor SSN altered the expression of Cox-2 in HT29
cells. To determine that the higher levels of apoptosis in HT29 cells with SC
236 >75 μM were related to decreased Cox-2 protein levels, we decreased Cox-2 protein expression in HT29 cells with curcumin (diferuloylmethane) and studied its effect on SC 236-induced apoptosis. Curcumin augmented apoptosis induced by SC 236 in HT29 cells but not in Cox-2 lacking HCT116 cells. In conclusion, selective Cox-2 inhibitors can induce apoptosis independent of Cox-2 expression. However they may selectively target cells that express Cox-2 by decreasing their Cox-2 protein expression.
IT **170569-86-5**, SC 236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(Cox-2 is needed but not sufficient for apoptosis induced by Cox-2 selective inhibitors in colon cancer cells)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 20 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



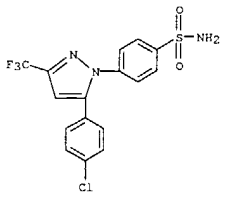
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:766726 CAPLUS
DOCUMENT NUMBER: 140:105110
TITLE: Differential antinociceptive effects induced by a selective cyclooxygenase-2 inhibitor (SC-236) on dorsal horn neurons and spinal withdrawal reflexes in anesthetized spinal rats
AUTHOR(S): You, H. J.; Morch, C. D.; Chen, J.; Arendt-Nielsen, L.
CORPORATE SOURCE: Center for Sensory-Motor Interaction, Laboratory for Experimental Pain Research, Aalborg University, Aalborg, DK-9220, Den.
SOURCE: Neuroscience (Oxford, United Kingdom) (2003), 121(2), 459-472
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of present study was to examine the effect of a selective cyclooxygenase-2 (COX-2) inhibitor SC-236 (4 mg/kg) on the simultaneous responsiveness of spinal wide-dynamic range (WDR) neurons and single motor units (SMUs) from gastrocnemius soleus muscles to mech. stimuli (pressure and pinch) and repeated suprathreshold (1.5*T, the intensity threshold) elec. stimuli with different frequencies (3 Hz, 20 Hz) under normal conditions and bee venom (BV, 0.2 mg/50 μl)-induced inflammation and central sensitization. During normal conditions, the responses of SMUs, but not WDR neurons, to mech. and repeated elec. stimuli (3 Hz, wind-up) were depressed by systemic administration of SC-236 as well as its vehicle (100% DMSO (DMSO)). The after-discharges of both the WDR neurons and the simultaneously recorded SMUs after elec. stimuli with 20 Hz were markedly depressed only by SC-236, indicating that the mechanisms underlying the generation of the C-fiber mediated late responses and the after-discharges may be different. The enhanced responsiveness of both WDR neurons and SMUs to mech. pressure stimuli (allodynia) and pinch stimuli (hyperalgesia) in the BV expts. was apparently depressed by SC-236, but not its vehicle. For elec. stimulation, the enhanced late responses and after-discharges, but not early responses, of both the WDR neurons and the simultaneously recorded SMUs were markedly depressed only by SC-236. This indicates that different central pharmacol. mechanisms underlie the generation of these enhanced early, late responses, and after-discharges during BV-induced inflammation. The data suggest that the COX-2 inhibitor SC-236 apparently depress the activities of both spinal cord dorsal horn neuron and spinal withdrawal reflex during BV-induced sensitization, indicating that COX-2 plays an important role in the maintenance of central sensitization.

IT **170569-86-5**, SC-236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential antinociceptive effects induced by COX-2 inhibitor (SC-236) on dorsal horn neurons and spinal withdrawal reflexes)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 21 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



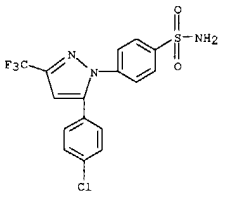
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:687464 CAPLUS
DOCUMENT NUMBER: 139:390968
TITLE: COX-2 Inhibitors Prolong Trauma-Induced Elevations of Iris Hyaluronan
AUTHOR(S): Koralewska-Makar, Anna; Johnsson, Cecilia; Bruun, Anitha; Stenevi, Ulf; Ehinger, Berndt
CORPORATE SOURCE: Department of Ophthalmology, University of Lund, Lund, Swed.
SOURCE: Journal of Ocular Pharmacology and Therapeutics (2003), 19(4), 385-395
CODEN: JOPTFU; ISSN: 1080-7683
PUBLISHER: Mary Ann Liebert, Inc..
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: To investigate whether and how treatment with COX-2 inhibitors influences hyaluronan responses to a standardized trauma, argon laser induced iritis, in rabbits. Methods: Two different COX-2 inhibitors were used, SC-236 and rofecoxib. The drugs were administered orally, 6 mg/kg/day and 1.5 mg/kg/day resp. Iris and aqueous humor hyaluronan concns. were measured with a radiometric assay at different time points after laser irradiation Results: The hyaluronan concentration in the iris increased 3-4-fold with a peak concentration of 129.1 μ g/g wet weight 2 days after laser irradiation It then decreased to normal values after 1 wk. In eyes treated with either of the COX-2 inhibitors, iris hyaluronan concns. did not decrease as rapidly and were significantly higher at day 4 and 7 when compared to drug untreated eyes. Conclusion: Treatment with COX-2 inhibitors prolongs trauma induced elevation of iris content of endogenous hyaluronan. This may be, at least partly, due to an inhibition of interstitial fluid pressure regulation.

IT **170569-86-5**, SC-236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2 inhibitors prolong trauma-induced elevations of iris hyaluronan)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 22 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



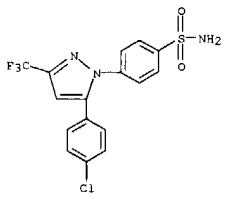
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:588176 CAPLUS
DOCUMENT NUMBER: 139:243902
TITLE: Inhibition of apoptosis in normal and transformed intestinal epithelial cells by cAMP through induction of inhibitor of apoptosis protein (IAP)-2
AUTHOR(S): Nishihara, Hiroshi; Kizaka-Kondoh, Shinae; Insel, Paul A.; Eckmann, Lars
CORPORATE SOURCE: Department of Pharmacology, University of California at San Diego, La Jolla, CA, 92093, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(15), 8921-8926
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclooxygenase (COX)-2, a rate-limiting enzyme of prostaglandin (PG) production, is overexpressed in colorectal adenomas and adenocarcinomas, and its inhibition by nonsteroidal antiinflammatory drugs protects against colorectal cancer. Mechanisms of cancer promotion by COX-2 are not fully understood, but signaling through prostaglandin (PG)E2 receptors is a contributing factor. The major PGE2 receptors on epithelial cells, EP2 and EP4, increase cAMP production, which promotes growth and inhibits apoptosis in some cell types. Here, the authors show that cAMP agonists, including PGE2, cholera toxin, and a membrane-permeant cAMP analog, protect normal and transformed intestinal epithelial cells from apoptosis induced by diverse stimuli. This protection is associated with cAMP-mediated, rapid induction of cellular inhibitor of apoptosis protein (c-IAP)-2 and delayed induction of LIVIN, but not of six other members of the IAP family. Concurrently and characteristic of IAP functions, the activity, but not generation, of the cleaved form of the central executioner caspase 3 is inhibited. Induction of c-IAP2 expression by cAMP agonists is accompanied by phosphorylation of cAMP response element binding protein and cAMP response element-dependent activation of transcriptional reporters. Furthermore, inhibition of COX-2 in cells overexpressing the enzyme decreases c-IAP2 expression and promotes apoptosis, both of which are reversible by PGE2 addition, suggesting that COX-2-promoted antiapoptosis is mediated by release of PGE2 and subsequent cAMP-dependent c-IAP2 induction. These results help to explain the cancer chemoprotective effects of nonsteroidal antiinflammatory drugs by defining a mechanism through which cAMP signaling can promote the development of colorectal and possibly other epithelial cancers by disruption of normal apoptotic processes.

IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of COX-2-dependent apoptosis in normal and transformed intestinal epithelial cells by PGE2-stimulated cAMP through induction of IAP-2 protein and cancer protective effects of nonsteroidal anti-inflammatory drugs)

L3 ANSWER 23 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:570814 CAPLUS
DOCUMENT NUMBER: 139:138734
TITLE: Use of COX-2 inhibitors in combination with antiviral agents for the treatment of papilloma virus infections
INVENTOR(S): Chong, Kong Teck
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

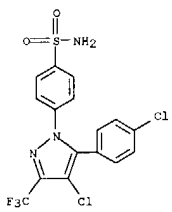
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059347	A1	20030724	WO 2003-US16	20030110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003211163	A1	20031113	US 2003-339906	20030110
PRIORITY APPLN. INFO.:			US 2002-347550P P	20020110

OTHER SOURCE(S): MARPAT 139:138734

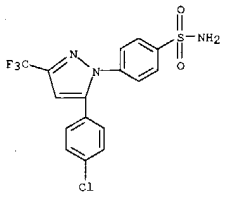
AB A method of treating papilloma virus infections comprising administering topically a cyclooxygenase-2 (COX-2) inhibitor or its pharmaceutically acceptable salt in combination with an antiviral agent. An antiviral agent is selected from a podophyllin, a nucleoside analog, an immunomodulator, an antisense oligonucleotide, or a vaccine. For example, celecoxib and valdecoxib topical compns. were prepared in ethanol using 5% parecoxib as a permeation enhancer. The presence of parecoxib enhanced the flux of celecoxib and valdecoxib across the cadaver skin membrane by factor of 11.5 and 8.4, resp.

IT **170569-50-3 170569-86-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical COX-2 inhibitors in combination with antiviral agents for treatment of papilloma virus infections)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 24 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

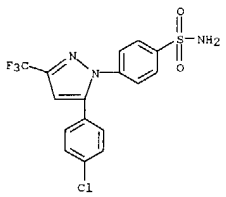
L3 ANSWER 25 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:492716 CAPLUS
DOCUMENT NUMBER: 139:63316
TITLE: Methods using a combination of a 3-heteroaryl-2-indolinone and a cyclooxygenase-2 inhibitor for the treatment of neoplasia
INVENTOR(S): Masferrer, Jaime L.; Cherrington, Julie M.; Leahy, Kathleen M.; Zweifel, Ben S.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of Appl. No. PCT/US99/30693.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003119895	A1	20030626	US 2002-150546	20020516
WO 2000038730	A2	20000706	WO 1999-US30693	19991222
WO 2000038730	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2003097044	A1	20031127	WO 2003-US15582	20030515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

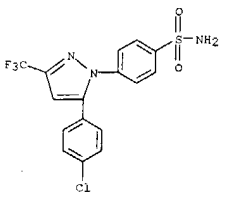
PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30693 A2 19991222
US 2002-150546 A 20020516

OTHER SOURCE(S): MARPAT 139:63316
AB The invention provides methods and compns. useful for treatment or prevention of neoplasia by administering a combination comprising a 3-heteroaryl-2-indolinone compound (preparation included) and a COX-2 selective inhibitor. Further provided are compns., pharmaceutical compns., and kits

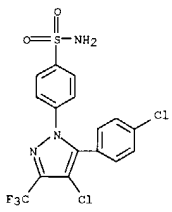
L3 ANSWER 25 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



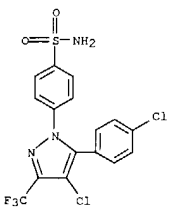
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 25 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
for treatment and prevention of neoplasia.
IT **170569-50-3 170569-50-3D**, prodrug derivs.
170569-86-5 170569-86-5D, prodrug derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heteroaryl indolinone-cyclooxygenase 2 inhibitor combination for treatment of neoplasia)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



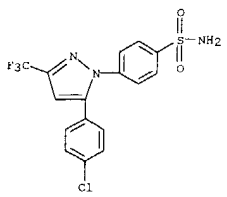
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 26 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:422753 CAPLUS
DOCUMENT NUMBER: 139:358300
TITLE: Nonsteroidal antiinflammatory drugs and a selective cyclooxygenase 2 inhibitor uncouple mitochondria in intact cells
AUTHOR(S): Krause, Manja M.; Brand, Martin D.; Krauss, Stefan; Meisel, Christian; Vergin, Hartmut; Burmester, Gerd-Rudiger; Buttgereit, Frank
CORPORATE SOURCE: University Hospital Charite, Humboldt-University Berlin, Berlin, Germany
SOURCE: Arthritis & Rheumatism (2003), 48(5), 1438-1444
CODEN: ARHEAW; ISSN: 0004-3591
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Uncoupling of isolated mitochondria by nonsteroidal antiinflammatory drugs (NSAIDs) has been considered relevant to the development of gastrointestinal (GI) side effects. We investigated the occurrence of NSAID-induced uncoupling of mitochondria in intact cells (rat thymocytes) compared with the effects of a selective cyclooxygenase 2 (COX-2) inhibitor. Oxygen consumption and mitochondrial membrane potential were simultaneously measured amperometrically and by distribution of radioactive tracer mols., resp., in the presence and absence of pharmacol. relevant concns. of the NSAIDs indomethacin and diclofenac and the selective COX-2 inhibitor SC-236. Anal. of data by a technique related to top-down elasticity anal. permitted assessment of the influence of these compds. on individual components of cellular energy metabolism Indomethacin, diclofenac, and SC-236 increased proton leak in isolated mitochondria. Both diclofenac and SC-236 significantly stimulated proton leak in intact cells and simultaneously inhibited substrate oxidation and ATP turnover. Oxygen consumption rates of isolated cells remained unchanged over a wide concentration range of the drugs, despite significant effects on subsystems of cellular energy metabolism. NSAIDs and selective COX-2 inhibitors have significant and equally directed effects on cellular energy metabolism They both uncouple mitochondrial respiration and inhibit substrate oxidation and ATP turnover. However, the topical effect and selective COX-2 inhibition may not be sufficient to cause NSAID-like damage to the GI tract.
IT **170569-86-5**, SC-236
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NSAIDs and selective cyclooxygenase 2 inhibitor uncouple mitochondria in intact cells)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 26 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
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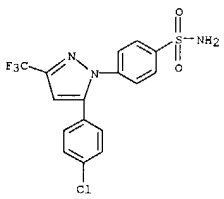
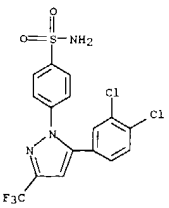
L3 ANSWER 27 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:370723 CAPLUS
DOCUMENT NUMBER: 139:374217
TITLE: QSAR study by Fujita-Ban model of some substituted α, β-diaryl five-membered heterocycles as COX-1/COX-2 inhibitors
AUTHOR(S): Sarathy, K. P.; Giridhar, R.; Yadav, M. R.
CORPORATE SOURCE: Pharmacy Department, Faculty of Technology and Engineering, The M.S. University of Baroda, Vadodara, 390 001, India
SOURCE: Indian Drugs (2003), 40(1), 9-18
CODEN: INDRBA; ISSN: 0019-462X
PUBLISHER: Indian Drug Manufacturers' Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three series of compds. namely, diaryloxazolones, diarylimidazoles and diarylpyrazoles were selected from literature to study the impact of different groups at various positions in rings A, B and C of the skeletons on cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) inhibitory activities. Fujita-Ban model of QSAR was performed on compds. of these series to identify the groups/ring systems selective for COX-1 or COX-2 inhibiting activities. A significant separation in both the activities could not be achieved by various substituents in rings A and B. In ring-C, methylsulfonyl has given a better separation of COX-1 and COX-2 activities in favor of more COX-2 enzyme inhibition. The results are indicative of more selective inhibition of COX-2 enzyme by diarylimidazoles than the remaining two series. On the basis of this study it is suggested that diarylimidazole ring system could provide more selective COX-2 inhibitors.
IT **170569-86-5 170569-92-3 170569-94-5 477801-74-4**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(QSAR study by Fujita-Ban model of some substituted α,β-diaryl five-membered heterocycles as COX-1/COX-2 inhibitors)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

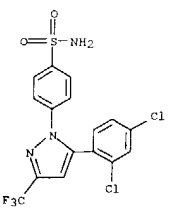
L3 ANSWER 27 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



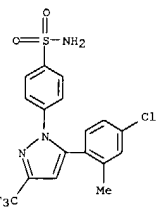
RN 170569-92-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-94-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

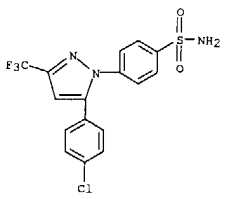


L3 ANSWER 27 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 477801-74-4 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chloro-2-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



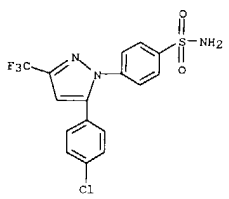
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 28 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:273883 CAPLUS
DOCUMENT NUMBER: 139:345429
TITLE: Combination of a Selective Cyclooxygenase-2 Inhibitor with Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor ZD1839 and Protein Kinase A Antisense Causes Cooperative Antitumor and Antiangiogenic Effect
AUTHOR(S): Tortora, Giampaolo; Caputo, Rosa; Damiano, Vincenzo; Melisi, Davide; Bianco, Roberto; Fontanini, Gabriella; Veneziani, Bianca Maria; De Placido, Sabino; Bianco, A. Raffaele; Ciardiello, Fortunato
CORPORATE SOURCE: Dipartimento di Endocrinologia e Oncologia Molecolare e Clinica, Universita di Napoli Federico II, Naples, 80131, Italy
SOURCE: Clinical Cancer Research (2003), 9(4), 1566-1572
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epidermal growth factor receptor (EGFR) and protein kinase A type I (PKAI) play an important role in the control of cancer cell growth and angiogenesis. Inhibitors of EGFR and PKAI have antitumor activity in vitro and in vivo in a variety of tumor types, and some of these agents are active after oral administration. Increasing evidence shows that cyclooxygenase (COX)-2 also plays a role in promoting cancer cell proliferation and angiogenesis. COX-2 expression can be induced by EGFR activation and is regulated by cAMP and PKA. Combination of an EGFR inhibitor with a non-selective COX-1/COX-2 inhibitor prevents the development of intestinal cancer in nude mice. Therefore, we investigated whether any cooperative antitumor effect can be obtained by the combined blockade of COX-2, EGFR, and PKAI. The COX-2 inhibitor SC-236 was combined with the selective EGFR tyrosine kinase inhibitor ZD1839 (Iressa) and the DNA/RNA-mixed backbone oligonucleotide AS-PKAI to study their effect on human cancer growth and angiogenesis, measuring vascular endothelial growth factor (VEGF) and basic fibroblast growth factor expression and vessel formation, in vitro and after oral administration of these agents in mice. A cooperative effect was observed with SC-236 in combination with either ZD1839 or AS-PKAI, as well as with all three agents together, on the proliferation of human colon and breast cancer cells in soft agar at doses that were ineffective for each agent alone. The antiproliferative effect was accompanied by inhibition of COX-2 expression. Moreover, combination of SC-236 with either agent or the triple combination markedly reduced VEGF secretion in the conditioned medium and completely suppressed VEGF and basic fibroblast growth factor expression. In nude mice bearing human colon cancer xenografts, a low, non-ID of SC-236 with ZD1839 and AS-PKAI, all given p.o., caused a dramatic cooperative antitumor effect, with no histol. evidence of tumor in 60% of mice 5 wk after treatment withdrawal, at which time all mice were alive. Moreover, anal. of tumor specimens revealed inhibition of vessel formation and expression of COX-2 and VEGF. This is the first demonstration that three novel agents blocking multiple signaling pathways, in absence of cytotoxic drugs, may have a potent antitumor and antiangiogenic activity after oral administration. Because all agents are under clin. evaluation, our results provide a rationale to translate this feasible therapeutic strategy into a clin. setting.
IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of a selective cyclooxygenase-2 (COX-2) inhibitor (SC-236) with EGF receptor tyrosine kinase inhibitor (ZD1839) and PKA antisense oligonucleotide causes cooperative antitumor and antiangiogenic effect)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



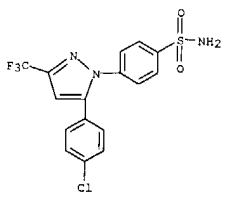
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 29 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:273837 CAPLUS
DOCUMENT NUMBER: 139:345023
TITLE: Molecular Therapeutics: Is One Promiscuous Drug against Multiple Targets Better than Combinations of Molecule-specific Drugs?
AUTHOR(S): Arteaga, Carlos L.
CORPORATE SOURCE: Vanderbilt-Ingram Comprehensive Cancer Center, Departments of Medicine and Cancer Biology, and Breast Cancer Program, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA
SOURCE: Clinical Cancer Research (2003), 9(4), 1231-1232
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, discussing the benefits and disadvantages of two different approaches to mol.-targeted therapeutics, i.e., the use of promiscuous small mol. inhibitors acting against multiple targets, such as ZD6474, SU6668, or STI-571, vs. combinations of inhibitors, such as ZD1839, SC-236, and antisense oligonucleotide against protein kinase A type I that work together in an additive or synergistic way.
IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benefits and disadvantages of two approaches to mol. therapeutics comparing promiscuous drugs against multiple targets with combinations of mol.-specific drugs)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 30 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:228533 CAPLUS
DOCUMENT NUMBER: 139:111218
TITLE: 15-Lipoxygenase-1 mediates cyclooxygenase-2 inhibitor-induced apoptosis in gastric cancer
AUTHOR(S): Wu, Jing; Xia, Harry Hua Xiang; Tu, Shui Ping; Fan, Dai Ming; Lin, Marie Chia Mi; Kung, Hsiang Fu; Lam, Shiu Kum; Wong, Benjamin Chun Yu
CORPORATE SOURCE: Dep. Med., Fourth Mil. Med. Univ., Xian, Peop. Rep. China
SOURCE: Carcinogenesis (2003), 24(2), 243-247
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was found that expression of 15-lipoxygenase-1 (15-LOX-1) and its main product, 13-S-hydroxyoctadecadienoic acid (13-S-HODE), are decreased in human colorectal and esophageal cancers and that non-steroidal anti-inflammatory drugs (NSAIDs) can therapeutically induce 15-LOX-1 expression to trigger apoptosis in those cancer cells. The authors found that a specific cyclooxygenase-2 (COX-2) inhibitor SC-236 similarly induced apoptosis in gastric cancer cells. In the present study, the authors tested whether SC-236 induced apoptosis through up-regulation of 15-LOX-1 in gastric cancer. The authors found that: (i) SC-236 inhibited growth of gastric cancer cells mainly by inducing apoptosis; (ii) SC-236 induced 15-LOX-1 expression and increased endogenous 13-S-HODE product, instead of 15-S-HETE during apoptosis; (iii) SC-236 did not affect expression of COX-1, COX-2, 5-LOX and 12-LOX; and (iv) 15-LOX-1 inhibition suppressed SC-236 induced apoptosis. These findings demonstrated that SC-236 induced apoptosis in gastric cancer cells via up-regulation of 15-LOX-1, and 13-S-HODE. These are potential and new targets for prevention and treatment of gastric cancer.
IT **170569-86-5**, SC-236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(15-LOX-1 mediates COX-2 inhibitor-induced apoptosis in gastric cancer)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 30 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

24/09/200410700019

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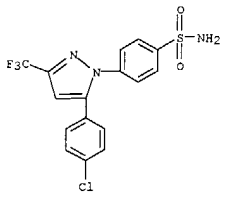
L3 ANSWER 30 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:228533 CAPLUS
DOCUMENT NUMBER: 139:111218
TITLE: 15-Lipoxygenase-1 mediates cyclooxygenase-2 inhibitor-induced apoptosis in gastric cancer
AUTHOR(S): Wu, Jing; Xia, Harry Hua Xiang; Tu, Shui Ping; Fan, Dai Ming; Lin, Marie Chia Mi; Kung, Hsiang Fu; Lam, Shiu Kum; Wong, Benjamin Chun Yu
CORPORATE SOURCE: Dep. Med., Fourth Mil. Med. Univ., Xian, Peop. Rep. China
SOURCE: Carcinogenesis (2003), 24(2), 243-247
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was found that expression of 15-lipoxygenase-1 (15-LOX-1) and its main product, 13-S-hydroxyoctadecadienoic acid (13-S-HODE), are decreased in human colorectal and esophageal cancers and that non-steroidal anti-inflammatory drugs (NSAIDs) can therapeutically induce 15-LOX-1 expression to trigger apoptosis in those cancer cells. The authors found that a specific cyclooxygenase-2 (COX-2) inhibitor SC-236 similarly induced apoptosis in gastric cancer cells. In the present study, the authors tested whether SC-236 induced apoptosis through up-regulation of 15-LOX-1 in gastric cancer. The authors found that: (i) SC-236 inhibited growth of gastric cancer cells mainly by inducing apoptosis; (ii) SC-236 induced 15-LOX-1 expression and increased endogenous 13-S-HODE product, instead of 15-S-HETE during apoptosis; (iii) SC-236 did not affect expression of COX-1, COX-2, 5-LOX and 12-LOX; and (iv) 15-LOX-1 inhibition suppressed SC-236 induced apoptosis. These findings demonstrated that SC-236 induced apoptosis in gastric cancer cells via up-regulation of 15-LOX-1, and 13-S-HODE. These are potential and new targets for prevention and treatment of gastric cancer.
IT **170569-86-5**, SC-236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(15-LOX-1 mediates COX-2 inhibitor-induced apoptosis in gastric cancer)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 30 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

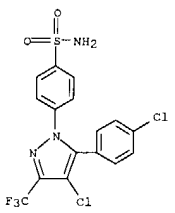
L3 ANSWER 31 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:154262 CAPLUS
DOCUMENT NUMBER: 138:198610
TITLE: Compositions for the treatment and prevention of pain and inflammation with a cyclooxygenase-2 selective inhibitor and chondroitin sulfate
INVENTOR(S): Pulaski, Steven P.; Kundel, Susan
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015799	A1	20030227	WO 2002-US25673	20020813
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003144416	A1	20030619	US 2002-215539	20020809
EP 1416941	A1	20040512	EP 2002-773188	20020813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

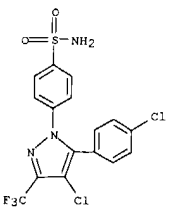
PRIORITY APPLN. INFO.: US 2001-312211P P 20010814
US 2002-215539 A 20020809
WO 2002-US25673 W 20020813

OTHER SOURCE(S): MARPAT 138:198610
AB A method of treating, preventing, or inhibiting pain, inflammation, or inflammation-associated disorder in a subject in need of such treatment or prevention includes treating the subject with chondroitin sulfate and a cyclooxygenase-2 selective inhibitor, or a prodrug thereof, wherein the amount of chondroitin sulfate and the amount of a cyclooxygenase-2 selective inhibitor or a pharmaceutically acceptable salt or prodrug thereof together constitute a pain- or inflammation-suppressing treatment or prevention effective amount. Glucosamine can optionally be present. Compns. that contain the combination of chondroitin sulfate and cyclooxygenase-2 selective inhibitor and, optionally, the glucosamine, are disclosed, as are pharmaceutical compns.
IT **170569-50-3** **170569-50-3D**, prodrug derivs.
170569-86-5 **170569-86-5D**, prodrug derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor and chondroitin sulfate for treatment and prevention of pain and inflammation)

L3 ANSWER 31 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

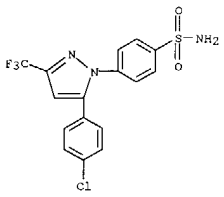


RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

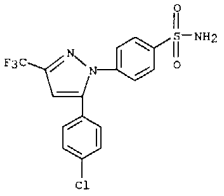


RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 31 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

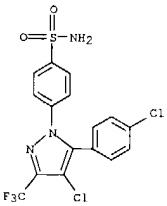


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

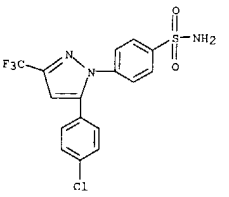
L3 ANSWER 32 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:154260 CAPLUS
DOCUMENT NUMBER: 138:198609
TITLE: Compositions for the treatment and prevention of pain and inflammation with a cyclooxygenase-2 selective inhibitor and glucosamine
INVENTOR(S): Pulaski, Steven P.; Kundel, Susan
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015797	A1	20030227	WO 2002-US25674	20020813
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003114418	A1	20030619	US 2002-215816	20020809
EP 1416940	A1	20040512	EP 2002-768522	20020813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:			US 2001-312272P	P 20010814
			US 2002-215216	A 20020809
			US 2002-215816	A 20020809
			WO 2002-US25674	W 20020813

OTHER SOURCE(S): MARPAT 138:198609
AB A method of treating, preventing, or inhibiting pain, inflammation or inflammation-associated disorder in a subject in need of such treatment or prevention provides for treating the subject with glucosamine and a cyclooxygenase-2 selective inhibitor or prodrug thereof, wherein the amount of glucosamine and the amount of a cyclooxygenase-2 selective inhibitor or prodrug thereof together constitute a pain or inflammation suppressing treatment or prevention effective amount of the composition Compns. and pharmaceutical compns. that contain glucosamine and a cyclooxygenase-2 selective inhibitor are also disclosed.
IT **170569-50-3 170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment and prevention of pain and inflammation with formulations contg. cyclooxygenase-2 selective inhibitors and glucosamine)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide,
4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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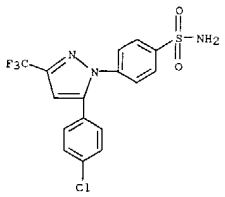
L3 ANSWER 33 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:148942 CAPLUS
DOCUMENT NUMBER: 139:111194
TITLE: Suppression of RelA/p65 nuclear translocation independent of IκB-α degradation by cyclooxygenase-2 inhibitor in gastric cancer
AUTHOR(S): Wong, Benjamin Chun Yu; Jiang, Xiao Hua; Fan, Xiao Ming; Lin, Marie Chia Mi; Jiang, Shi Hu; Lam, Shiu Kum; Kung, Hsiang Fu
CORPORATE SOURCE: Dep. Med., Univ. Hong Kong, Hong Kong
SOURCE: Oncogene (2003), 22(8), 1189-1197
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Selective cyclooxygenase-2 (COX-2) inhibitors are promising anti-inflammatory drugs with potential antitumor activities. The nuclear factor-kappa B (NF-κB) family of proteins is important transcriptional regulators of genes involved in immunity, inflammation, and carcinogenesis. In the present study, we investigated whether and by which mol. mechanism the selective COX-2 inhibitors inhibit NF-κB activation in gastric cancer. The effects of SC236 and its derivative, but devoid of COX-2 enzyme inhibition activity on NF-κB signaling, were evaluated using electromobility shift, transfection, and reporter gene assay. The translocation of RelA/p65 was investigated using Western blotting and immunocytochem. We showed that SC236 suppressed NF-κB-mediated gene transcription and binding activity in gastric cancer. This effect occurred through a mechanism independent of cyclooxygenase activity and prostaglandin synthesis. Furthermore, unlike aspirin, SC236 affected neither the phosphorylation, degradation, nor expression of IκB-α, suggesting that the effects of SC236 are independent of IKK activity and IκB-α gene transcription. Instead, SC236 worked directly through suppressing nuclear translocation of RelA/p65. It is possible that SC236 directly targets proteins that facilitate the nuclear translocation of NF-κB. Our study suggests an important mol. mechanism by which COX-2 inhibitors reduce inflammation and suppress carcinogenesis in gastrointestinal tract.
IT **170569-86-5**, SC236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppression of RelA/p65 nuclear translocation independent of IκB-α degradation by COX-2 inhibitor in gastric cancer)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 33 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



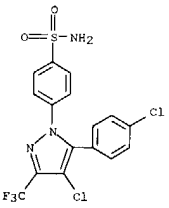
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 34 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:43025 CAPLUS
DOCUMENT NUMBER: 138:83362
TITLE: Methods of using a combination of cyclooxygenase-2 selective inhibitors and thalidomide for the treatment
of neoplasia
INVENTOR(S): Masferrer, Jaime L.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of U. S. Ser. No. 470,951.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

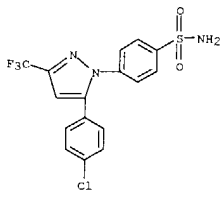
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003013739	A1	20030116	US 2002-135793	20020430
WO 2003092691	A1	20031113	WO 2003-US13080	20030425
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
BR 2003004648	A	20040803	BR 2003-4648	20030425
PRIORITY APPLN. INFO.:			US 1998-113786P	P 19981223
			US 1999-470951	A2 19991222
			US 2002-135793	A 20020430
			WO 2003-US13080	W 20030425

OTHER SOURCE(S): MARPAT 138:83362
AB The present invention provides compns. and methods for the treatment, prevention or inhibition of neoplasia by administering an effective amount
of a cyclooxygenase-2 selective inhibitor in combination with an effective
amount of thalidomide.
IT **170569-50-3 170569-86-5**, 4-[5-(4-Chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor; combination of cyclooxygenase-2 selective inhibitors and thalidomide for treatment of neoplasia)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide,
4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-

L3 ANSWER 34 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 35 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:942791 CAPLUS
DOCUMENT NUMBER: 138:14058
TITLE: Preparation of pyrazolylbenzenesulfonamides as cyclooxygenase inhibitors for treatment of inflammation.
INVENTOR(S): Talley, John J.; Penning, Thomas D.; Collins, Paul W.;
Rogier, Donald J., Jr.; Malecha, James W.; Miyashiro, Julie M.; Bertenshaw, Stephen R.; Khanna, Ish K.; Graneto, Matthew J.; Rogers, Roland S.; Carter, Jeffery S.; Docter, Stephen H.; Yu, Stella S.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 55 pp., Cont.-in-part of U.S. 6,413,960.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6492411	B1	20021210	US 2002-125325	20020417
US 5466823	A	19951114	US 1993-160594	19931130
US 5521207	A	19960528	US 1994-223629	19940406
WO 9515316	A1	19950608	WO 1994-US12720	19941114
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5760068	A	19980602	US 1996-648113	19960906
US 6156781	A	20001205	US 1999-449076	19991124
US 6413960	B1	20020702	US 2000-609011	20000530
US 6586603	B1	20030701	US 2002-274679	20021021
US 6716991	B1	20040406	US 2003-378781	20030304
PRIORITY APPLN. INFO.:			US 1993-160594	A2 19931130
			US 1994-223629	A1 19940406
			WO 1994-US12720	A1 19941114
			US 1996-648113	A1 19960906
			US 1997-957345	B1 19971024
			US 1999-449076	A1 19991124
			US 2000-609011	A2 20000530
			US 2002-125325	A1 20020417
			US 2002-274679	A1 20021021

OTHER SOURCE(S): MARPAT 138:14058
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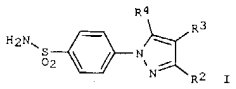
L3 ANSWER 35 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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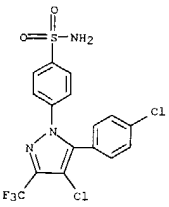
AB A method for the treatment of headache comprises administration of an asthma treating-effective amount of title compds. [I; R2 = H, alkyl, haloalkyl, alkoxycarbonyl, cyano, cyanoalkyl, CO2H, aminocarbonyl, alkylaminocarbonyl, cycloalkylaminocarbonyl, arylaminocarbonyl, carboxyalkylaminocarbonyl, carboxyalkyl, aralkoxycarbonylalkylaminocarbony l, aminocarbonylalkyl, alkoxycarbonylcyanoalkenyl hydroxyalkyl; R3 = H, alkyl, cyano, hydroxyalkyl, cycloalkyl, alkylsulfonyl, halo; R4 = aralkenyl, aryl, cycloalkyl, cycloalkenyl heterocyclic; R4 is optionally substituted with ≥1 of alkylthio, alkylsulfonyl, cyano, nitro, haloalkyl, alkyl, OH, alkenyl, hydroxyalkyl, CO2H, cycloalkyl, alkylamino, dialkylamino, alkoxycarbonyl, aminocarbonyl, alkoxy, haloalkoxy, sulfamyl, heterocyclyl, amino; provided R2 and R3 are not both H; further provided that R2 ≠ CO2H or Me when R3 = H and when R4 = Ph; further provided that R4 ≠ triazolyl when R2 = Me; further provided that R4 ≠ aralkenyl when R2 = carboxyl, aminocarbonyl, ethoxycarbonyl; further provided that R4 ≠ Ph when R2 = Me and R3 = CO2H; and further provided that R4 ≠ unsubstituted thienyl when R2 = CF3], is claimed. Thus, 4,4,4-trifluoro-1-[4-(chloro)phenyl]butane-1,3-dione (preparation given) 4-sulfonamidophenylhydrazine hydrochloride were refluxed 20 h in EtOH to give 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide. The latter at 10 mg/kg gave 44% inhibition in the rat paw edema test.

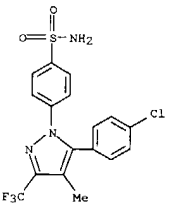
IT **170569-50-3P 170569-54-7P 170569-55-8P 170569-86-5P**, 4-[5-(4-Chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide **170569-92-3P 170569-94-5P 170570-07-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazolylbenzenesulfonamides as cyclooxygenase inhibitors for treatment of inflammation)

RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 35 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

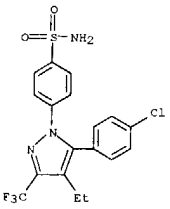


RN 170569-54-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

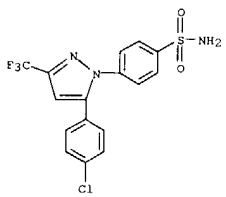


RN 170569-55-8 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-ethyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

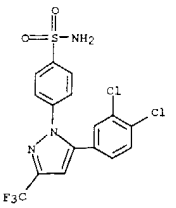
L3 ANSWER 35 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

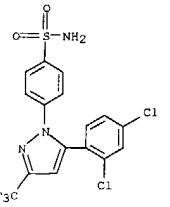


RN 170569-92-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

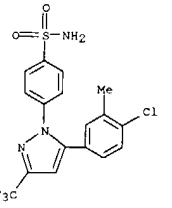


L3 ANSWER 35 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 170569-94-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



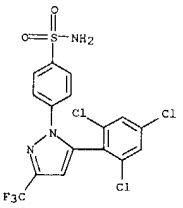
RN 170570-07-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chloro-3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



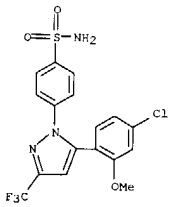
IT **477801-64-2 477801-68-6 477801-74-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pyrazolylbenzenesulfonamides as cyclooxygenase inhibitors for treatment of inflammation)

RN 477801-64-2 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4,6-trichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 35 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

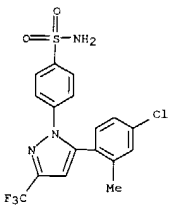


RN 477801-68-6 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chloro-2-methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 477801-74-4 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chloro-2-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 35 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 36 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN

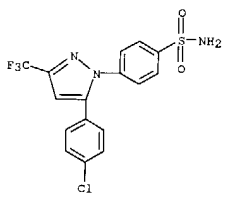
ACCESSION NUMBER: 2002:937162 CAPLUS
DOCUMENT NUMBER: 139:127381
TITLE: Using Cyclooxygenase-2 Inhibitors as Molecular Platforms to Develop a New Class of Apoptosis-Inducing Agents
AUTHOR(S): Zhu, Jiuxiang; Song, Xueqin; Lin, Ho-Pi; Young, Donn C.; Yan, Shunqi; Marquez, Victor E.; Chen, Ching-Shih
CORPORATE SOURCE: College of Pharmacy, Division of Medicinal Chemistry and Pharmacognosy, The Ohio State University, Columbus, OH, USA
SOURCE: Journal of the National Cancer Institute (2002), 94(23), 1745-1757
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:127381

AB Background: The cyclooxygenase-2 (COX-2) inhibitor celecoxib is thought to act as a chemopreventive agent by sensitizing cancer cells to apoptotic signals. Other COX-2 inhibitors, such as rofecoxib, are two orders of magnitude less potent than celecoxib at inducing apoptosis. The mol. structures of celecoxib and rofecoxib were used as starting points to examine the structural features that contribute to this discrepancy. Methods: the authors used a systematic chemical approach to modify the structures of celecoxib and rofecoxib to produce a series of compds. that were tested for their effects on the viability of human prostate cancer PC-3 cells and their ability to induce apoptosis in these cells. Cell viability was measured by the trypan blue dye exclusion assay, and apoptosis was measured by an ELISA that quantifies DNA cleavage and by western blot detection of poly(ADP-ribose) polymerase (PARP) cleavage. Western blotting was used to monitor the effects of the compds. on phosphorylation of the serine/threonine kinase Akt and extracellular signal-regulated kinase 2 (ERK2), two components of celecoxib-induced apoptosis signaling. Monte Carlo simulations were used to molecularly model the surface electrostatic potential and electron d. of selected compds. All statistical tests were two-sided. Results: The structural requirements for the induction of apoptosis in PC-3 cells were different from those for COX-2 inhibition. Structure-function anal. indicated that the induction of apoptosis by compds. derived from COX-2 inhibitors required a bulky terminal Ph ring, a heterocyclic system with neg. electrostatic potential, and a benzenesulfonamide or benzenecarboxamide moiety. These derivs. mediated apoptosis by facilitating the dephosphorylation of Akt and ERK2, irresp. of their COX-2 inhibitory activities. Conclusion: A new class of compds. that induce apoptosis by targeting Akt and ERK2 signaling pathways in human prostate cancer cells can be synthesized by modifying existing COX-2 inhibitors.

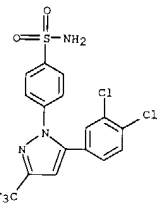
IT **170569-86-5 170569-92-3 170569-94-5**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(using cyclooxygenase-2 inhibitors as mol. platforms to develop new class of apoptosis-inducing agents that target Akt and ERK2 signaling pathways in human prostate cancer cells)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

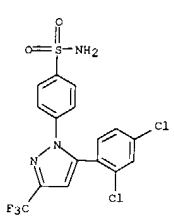
L3 ANSWER 36 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-92-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

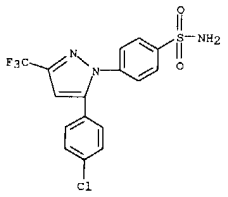


RN 170569-94-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 36 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 37 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:933905 CAPLUS
DOCUMENT NUMBER: 139:78720
TITLE: COX inhibition in the rat knee joint
AUTHOR(S): Egan, C. G.; Lockhart, J. C.; Ferrell, W. R.
CORPORATE SOURCE: Division of Biological Sciences, University of Paisley, UK
SOURCE: World Congress for Microcirculation, submitted Papers,
7th, Sydney, Australia, Aug. 19-22, 2001 (2001), 333-336. Monduzzi Editore: Bologna, Italy.
CODEN: 69DILJ; ISBN: 88-323-1819-9
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Transcutaneous laser Doppler imaging (LDI) was used to measure perfusion changes in the normal and acutely inflamed rat knee joint. The i.v. infusion of indomethacin (a non-selective COX inhibitor; 0.34 nmol/min) significantly increased vascular resistance in normal and inflamed knees. An equimolar concentration of SC-236 (selective COX-2 inhibitor) did not significantly alter resistance in the normal or 24 h inflamed joint. These findings demonstrate that COX-1 has a physiol. role in the joint, and that unlike the development of inflammatory hyperemia, basal perfusion
in the inflamed joint at 24 h is not dependent on COX-2.
IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); BIOL (Biological study)
(COX inhibition effect on vascular resistance in normal and inflamed rat knee joint)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



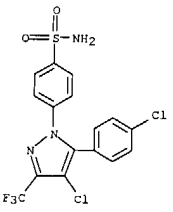
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 38 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:927290 CAPLUS
DOCUMENT NUMBER: 138:11413
TITLE: Use of cyclooxygenase-2 selective inhibitors and radiation for inhibition or prevention of cardiovascular disease
INVENTOR(S): Keller, Patricia G.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

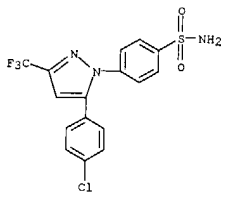
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096516	A1	20021205	WO 2002-US17552	20020529
WO 2002096516	C1	20030220		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1406696	A1	20040414	EP 2002-739651	20020529
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002009776	A	20040713	BR 2002-9776	20020529
PRIORITY APPLN. INFO.:			US 2001-294077P	P 20010529
			WO 2002-US17552	W 20020529

OTHER SOURCE(S): MARPAT 138:11413
AB The invention discusses the use of cyclooxygenase-2 selective inhibitor with a dose of radiation for the prevention or inhibition of cardiovascular disease.
IT **170569-50-3 170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 selective inhibitors and radiation for inhibition or prevention of cardiovascular disease)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 38 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



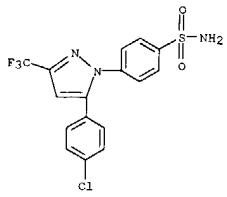
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 39 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:899403 CAPLUS
DOCUMENT NUMBER: 138:378831
TITLE: Selective inhibitors of cyclooxygenase-2 (COX-2) induce hypoalgesia in a rat paw model of inflammation
AUTHOR(S): Francischi, J. N.; Chaves, C. T.; Moura, A. C. L.; Lima, A. S.; Rocha, O. A.; Ferreira-Alves, D. L.; Bakhle, Y. S.
CORPORATE SOURCE: Departamento de Farmacologia, ICB, Universidade Federal de Minas Gerais, Belo Horizonte, CEP. 31270-901, Brazil
SOURCE: British Journal of Pharmacology (2002), 137(6), 837-844
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Paw edema and hyperalgesia in rats were induced by injecting carrageenan (250 μg) into a hindpaw. Both inflammatory responses were followed for 24 h after the injection, measuring hyperalgesia by decreased pain threshold in the paws and edema by plethysmog. Three selective inhibitors of COX-2: celecoxib, rofecoxib and SC 236, given systemically in a range of doses before the inflammatory stimulus, abolished carrageenan-induced hyperalgesia with little reduction of edema. These inhibitors also induced hypoalgesia, increasing nociceptive thresholds in the inflamed paw above normal, noninflamed values. This hypoalgesia was lost at the higher doses of the selective inhibitors, although hyperalgesia was still prevented. In paws injected with saline only, celecoxib, given at the dose inducing the maximum hypoalgesia after carrageenan, did not alter the nociceptive thresholds. Two nonselective inhibitors of COX-2, indomethacin and piroxicam, abolished hyperalgesia and reduced edema but did not induce hypoalgesia. Celecoxib given locally into the paw also abolished inflammatory hyperalgesia and induced hypoalgesia without reducing edema. It is concluded that hypoalgesia is expressed only over a critical range of COX-2 inhibition and that concomitant inhibition of COX-1 prevents expression of hypoalgesia, although hyperalgesia is still prevented. The results suggest a novel antinociceptive pathway mediating hypoalgesia, involving COX-2 selectively and having a clear peripheral component. This peripheral component can be further explored for therapeutic purposes.

IT **170569-86-5**, SC 236
RL: PAC (Pharmacological activity); BIOL (Biological study)
(selective cyclooxygenase-2 inhibitors such as SC 236 induction of hypoalgesia in a rat paw model of inflammation)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 39 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

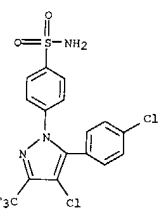
L3 ANSWER 40 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:777650 CAPLUS
DOCUMENT NUMBER: 137:299910
TITLE: Therapeutic combinations containing COX-2 inhibitors for cardiovascular and inflammatory diseases treatment
INVENTOR(S): Seibert, Karen; Keller, Bradley T.; Isakson, Peter C.; Krul, Elaine S.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 316 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078626	A2	20021010	WO 2002-US9346	20020328
WO 2002078626	A3	20040429		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003199482	A1	20031023	US 2002-107809	20020328
EP 1435956	A2	20040714	EP 2002-725362	20020328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004186154	A1	20040923	US 2004-473045	20040506
PRIORITY APPLN. INFO.:			US 2001-279239P P	20010328
			WO 2002-US9346 W	20020328

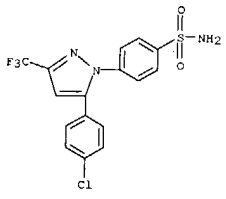
AB The present invention provides therapeutic combinations and methods for treating or preventing a hypercholesterolemia-related or an inflammation-related condition in a subject in need of such treatment or prevention. One therapeutic combination comprises an ASBT inhibitor combined with COX-2 inhibitor. A further therapeutic combination comprises an ASBT inhibitor, a COX-2 inhibitor and an HMG Co-A reductase inhibitor. Another therapeutic combination comprises a chromene COX-2 inhibitor and an HMG Co-A reductase inhibitor. Thus, a tablet composition contained benzothiepine 5, celecoxib 20, lactose 54, microcryst. cellulose 15, HPMC 3, Croscarmellose sodium 2, and Mg stearate 1 mg/tablet.

IT **170569-50-3 170569-86-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic combinations containing COX-2 inhibitors for cardiovascular and inflammatory diseases treatment)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 40 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



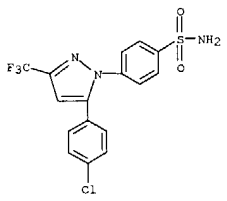
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 41 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:760152 CAPLUS
DOCUMENT NUMBER: 138:364821
TITLE: In vitro enhancement of tumor cell radiosensitivity by a selective inhibitor of Cyclooxygenase-2 enzyme: mechanistic considerations
AUTHOR(S): Raju, Uma; Nakata, Eiko; Yang, Peiying; Newman, Robert A.; Ang, Kian K.; Milas, Luka
CORPORATE SOURCE: Department of Experimental Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (2002), 54(3), 886-894
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: Selective cyclooxygenase-2 inhibitors have been reported to enhance the tumor response to radiation in vivo, but the cellular mechanisms underlying the radiosensitizing effect are not understood. In the present study, we investigated several possible mechanisms using a murine sarcoma cell culture system. Methods and Materials: Cells derived from a murine sarcoma, designated NFSA, were cultured in vitro and exposed to different (either single or split) doses of radiation with and without a pretreatment of SC-236 (4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl] benzene sulfonamide), a selective cyclooxygenase-2 (COX-2) inhibitor. The cells were assayed for clonogenic survival to determine the radiosensitizing effect of SC-236. In addition, MTT assay and TUNEL assay were performed to determine the effects of SC-236 and radiation on the cell survival and cell cycle distribution. RNase protection assay was performed on the total RNA extract using probes that encoded for selected cell cycle regulatory proteins, such as cyclins and cyclin-dependent kinases. To monitor the extent of COX-2 activity and its role in radiosensitization, the cellular content of prostaglandin E2, a major metabolite of COX-2 activity on arachidonic acid, was also determined Results: The cell clonogenic survival assay showed that SC-236 significantly enhanced tumor cell radiosensitivity: 50 M SC-236 increased it by a factor of 1.51 at the 0.1 cell survival level. Treatment with SC-236 (50 μM, 3 days) removed the "shoulder" region on the radiation survival curve, suggesting that the drug inhibited repair of sublethal radiation damage. The inhibition was confirmed by split-dose expts. where two doses (3 Gy each) of radiation were given 4 h apart. The cells exposed to radiation only repaired the damage by a factor of 1.44, whereas those treated with SC-236 plus radiation repaired it by a factor of 1.1 only. Whereas SC-236 induced apoptosis in these NFSA cells, radiation did not. No further increase in apoptosis was observed when the cells were exposed to both SC-236 and radiation, suggesting that SC-236 did not render tumor cells more susceptible to radiation-induced apoptosis. The RNase protection assay showed that SC-236 (50 μM, 3 days) inhibited the expression of cyclins A and B, as well as cyclin-dependent kinase-1. Inhibition of these cell cycle regulatory elements by SC-236 was assocd. with the arrest of cells in the radiosensitive G2-M phase (67%), detd. by flow cytometry. Conclusions: SC-236 significantly enhanced radiosensitivity of tumor cells; the magnitude of sensitivity was dependent on the drug's concn. The likely mechanisms involve accumulation of cells in the radiosensitive G2-M phase of the cell cycle and inhibition of repair from sublethal radiation damage.

IT **170569-86-5**, SC-236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cellular mechanisms for in vitro enhancement of tumor cell radiosensitivity by selective inhibitor of cyclooxygenase-2 enzyme)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

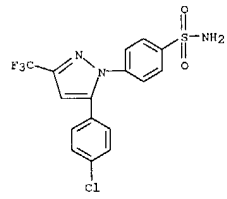
L3 ANSWER 42 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:716096 CAPLUS
DOCUMENT NUMBER: 137:226651
TITLE: Combined method for treating hormone-dependent disorders with aromatase inactivator exemestane and other therapeutic agents
INVENTOR(S): Di Salle, Enrico; Piscitelli, Gabriella; Massimini, Giorgio; Purandare, Dinesh; Dekoning, Gans Hendrik
PATENT ASSIGNEE(S): Pharmacia Italia S.p.A., Italy; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072106	A2	20020919	WO 2002-EP638	20020118
WO 2002072106	A3	20031030		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1377298	A2	20040107	EP 2002-727314	20020118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004519490	T2	20040702	JP 2002-571065	20020118
US 2004082557	A1	20040429	US 2003-611653	20030702

PRIORITY APPLN. INFO.: US 2001-770911 A 20010126
WO 2002-EP638 W 20020118
US 2002-393320P P 20020702

AB A method of preventing and treating estrogen dependent disorders selected from endometriosis, uterine fibroids, dysfunctional uterine bleeding, endometrial hyperplasia, polycystic ovarian disease, fibrocystic breast disease and fibrocystic mastopathy, is disclosed which is comprised of administering to a mammalian patient in need of such treatment an effective amount of aromatase inactivator exemestane, alone or in combination with addnl. therapeutic agents.

IT **170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined method for treating hormone-dependent disorders with aromatase inactivator exemestane and other therapeutic agents)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

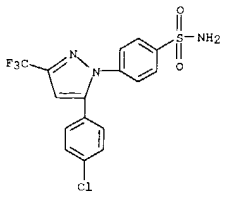


L3 ANSWER 43 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:655922 CAPLUS
DOCUMENT NUMBER: 138:248025
TITLE: Apo2L/TRAIL differentially modulates the apoptotic effects of sulindac and a COX-2 selective non-steroidal anti-inflammatory agent in Bax-deficient cells
AUTHOR(S): He, Qin; Luo, Xiuquan; Huang, Ying; Sheikh, M. Saeed
CORPORATE SOURCE: Department of Pharmacology, State University of New York, Upstate Medical University, Syracuse, New York, NY, 13210, USA
SOURCE: Oncogene (2002), 21(39), 6032-6040
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The nonsteroidal anti-inflammatory drugs (NSAIDs) are believed to mediate their anticancer effects by inducing apoptosis but the mol. mechanisms of their apoptotic effects remain largely unknown. Here the authors report that 2 different NSAIDs, sulindac sulfide and SC-'236 engage the death receptor 5 (DR5) and mitochondrial pathways to mediate apoptosis in human colon cancer cells. The authors show that sulindac sulfide and SC-'236-induced apoptosis is coupled with upregulation of DR5, caspase 8 activation and Bid cleavage. Thus, a cross talk appears to exist between the DR5 and mitochondrial pathways during apoptosis induced by these NSAIDs. The authors further show that sulindac sulfide and SC-'236-induced DR5 upregulation occurs independent of the COX inhibitory effects of these NSAIDs. Using Bax-proficient (Bax+/-) and Bax-deficient (Bax-/-) HCT116 human colon cancer cells, the authors further demonstrate that Apo2L/TRAIL differentially modulates the apoptotic effects of sulindac sulfide and SC-'236. For example, sulindac sulfide upregulates DR5 in both Bax-deficient and proficient cells, but Apo2L/TRAIL efficiently potentiates sulindac sulfide-induced apoptosis as well as activation of caspase-8, -9, and -3 only in Bax-proficient cells. SC-'236 also upregulates DR5 in both Bax-proficient and Bax-deficient cells but Apo2L/TRAIL potentiates SC-'236-mediated apoptosis and caspases-8 and -3 activation in both Bax-proficient and Bax-deficient cells. Further, in Bax-deficient cells, neither sulindac sulfide nor SC-'236 in combination with Apo2L/TRAIL effectively promotes the release of cytochrome c from mitochondria into cytosol and caspase-9 activation. Collectively, the authors' results suggest that unlike sulindac sulfide, SC-'236 in combination with Apo2L/TRAIL can overcome Bax deficiency to induce apoptosis. These results have important clin. implications in that the tumors harboring Bax mutations are likely to develop resistance to sulindac but not to SC-'236-like NSAIDs. In conclusion, the data presented herein form the basis of future in-depth studies to further explore the utility of Apo2L/TRAIL and NSAIDs, in combination, as a novel cancer preventive/therapeutic strategy.

IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Apo2L/TRAIL and NSAID-mediated apoptosis in Bax deficient cells)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 43 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



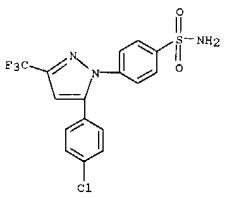
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 44 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:655915 CAPLUS
DOCUMENT NUMBER: 138:248023
TITLE: Novel target for induction of apoptosis by cyclo-oxygenase-2 inhibitor SC-236 through a protein kinase C-β1-dependent pathway
AUTHOR(S): Jiang, Xiao-Hua; Lam, Shiu-Kum; Lin, Marie C. M.; Jiang, Shi-Hu; Kung, Hsiang-Fu; Slosberg, Eric D.; Soh, Jae Won; Weinstein, I. Bernard; Wong, Benjamin Chun-Yu
CORPORATE SOURCE: Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, Peop. Rep. China
SOURCE: Oncogene (2002), 21(39), 6113-6122
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nonsteroidal anti-inflammatory drugs (NSAIDs) reduce the risk of gastrointestinal cancers. Recently, a similar protective effect was demonstrated by the specific cyclo-oxygenase-2 (COX-2) inhibitors. However, the exact mechanism that accounts for the anti-proliferative effect of specific COX-2 inhibitors is still not fully understood, and it is still controversial whether these protective effects are predominantly mediated through the inhibition of COX-2 activity and prostaglandin synthesis. Identification of mol. targets regulated by COX-2 inhibitors could lead to a better understanding of their pro-apoptotic and anti-neoplastic activities. In the present study, the authors investigated the effect and the possible mol. target of a COX-2-specific inhibitor SC-236 on gastric cancer. The authors showed that SC-236 induced apoptosis in gastric cancer cells. However, this effect was not dependent on COX-2 inhibition. SC-236 down-regulated the protein expression and kinase activity of PKC-β1, increased the expression of PKCδ and PKCη, but did not alter the expression of other PKC isoforms in AGS cells. Moreover, exogenous prostaglandins or PGE2 receptor antagonists could not reverse the inhibition effect on PKCβ1 by SC-236, which suggested that this effect occurred through a mechanism independent of cyclo-oxygenase activity and prostaglandin synthesis. Overexpression of PKCβ1 attenuated the apoptotic response of AGS cells to SC-236 and was associated with overexpression of p21waf1/cip1. Inhibition of PKCβ1-mediated overexpression of p21waf1/cip1 partially reduced the anti-apoptotic effect of PKCβ1. The down-regulation of PKCβ1 provides an explanation for COX-independent apoptotic effects of specific COX-2 inhibitor in cultured gastric cancer cells. The authors also suggest that PKCβ1 act as survival mediator in gastric cancer, and its down-regulation by COX-2 inhibitor SC-236 may provide new target for future treatment of gastric cancer.

IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel target for apoptosis induction by COX-2 inhibitor SC-236 through protein kinase C-β1-dependent pathway)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 44 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



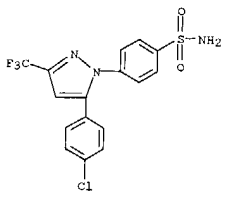
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 45 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:640195 CAPLUS
DOCUMENT NUMBER: 138:198519
TITLE: Cyclooxygenase-1-selective inhibition prolongs gestation in mice without adverse effects on the ductus arteriosus
AUTHOR(S): Loftin, Charles D.; Trivedi, Darshini B.; Langenbach, Robert
CORPORATE SOURCE: Laboratory of Environmental Carcinogenesis and Mutagenesis, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA
SOURCE: Journal of Clinical Investigation (2002), 110(4), 549-557
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Preterm delivery is the leading cause of neonatal mortality and contributes significantly to infant morbidity. Classical cyclooxygenase (COX) inhibitors, such as indomethacin, which inhibit both COX-1 and COX-2, are effective for delaying premature labor, but their use is limited by serious complications to the fetus and neonate, including adverse effects on the ductus arteriosus (DA). Using isoform-selective inhibitors, we characterized the roles of the COX isoforms in the initiation of labor and the regulation of fetal and neonatal DA closure in mice. Chronic inhibition of COX-2 during pregnancy (gestation days 15-18) significantly increased neonatal mortality by preventing closure of the DA after birth, whereas acute COX-2 inhibition near the end of term (gestation day 18) constricted the fetal DA. In contrast, the inhibition of COX-1 during pregnancy lacked these prenatal and postnatal adverse effects on the DA and effectively delayed the initiation of full-term labor and LPS-induced preterm labor. These findings suggest that premature fetal DA closure or neonatal patent DA observed following indomethacin tocolysis in women may result from the inhibition of COX-2. Therefore, COX-1-selective inhibitors may provide effective treatment to delay preterm labor with fewer adverse effects on fetal or neonatal health than nonselective or COX-2-selective inhibitors.

IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-1-selective inhibition prolongs gestation in mice without adverse effects on ductus arteriosus)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 45 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L3 ANSWER 46 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:575747 CAPLUS
DOCUMENT NUMBER: 137:135070
TITLE: DNA topoisomerase I inhibitor-cyclooxygenase 2 inhibitor antiangiogenic combination for the treatment of cancer
INVENTOR(S): McKearn, John P.; Gordon, Gary B.; Cunningham, James; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 97 pp., Cont.-in-part of U.S. Ser. No. 470,951.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103141	A1	20020801	US 2001-843132	20010425
WO 2002085459	A2	20021031	WO 2002-US13219	20020425
WO 2002085459	A3	20040304		
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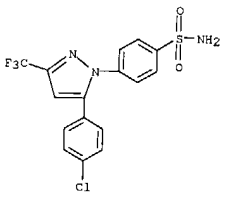
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1414526	A2	20040506	EP 2002-731524	20020425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002009269	A	20040622	BR 2002-9269	20020425
NO 2003004780	A	20031212	NO 2003-4780	20031024
US 2004127539	A1	20040701	US 2003-692643	20031024
PRIORITY APPLN. INFO.:			US 1998-113786P	P 19981223
			US 1999-470951	A2 19991222
			US 2001-843132	A 20010425
			WO 2002-US13219	W 20020425

OTHER SOURCE(S): MARPAT 137:135070

AB The invention provides combinations of a DNA topoisomerase I inhibiting agent and a selective COX-2 inhibiting agent for preventing, treating, and/or reducing the risk of developing a neoplasia disorder in a mammal. Compound preparation is included.

IT **170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA topoisomerase I inhibitor-cyclooxygenase 2 inhibitor antiangiogenic combination for treatment of cancer)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, [illegible]thyl)-1H-pyrazol-1-

L3 ANSWER 46 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
yl]- (9CI) (CA INDEX NAME)



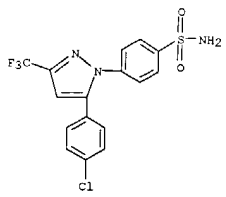
L3 ANSWER 47 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:546915 CAPLUS
DOCUMENT NUMBER: 138:234098
TITLE: Pronounced radiosensitization of cultured human cancer cells by COX inhibitor under acidic microenvironment
AUTHOR(S): Shah, Tushar; Ryu, Samuel; Lee, Ho Jun; Brown, Stephen; Kim, Jae Ho
CORPORATE SOURCE: Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI, USA
SOURCE: International Journal of Radiation Oncology, Biology, Physics (2002), 53(5), 1314-1318
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: To demonstrate the influence of pH on the cytotoxicity and radiosensitization by COX (cyclooxygenase) -1 and -2 inhibitors using established human cancer cells in culture. Methods and Materials: Nonselective COX inhibitor, ibuprofen (IB), and selective COX-2 inhibitor, SC-236, were used to determine the cytotoxicity and radiosensitization at varying pH of culture media. Human colon carcinoma cell line (HT-29) was exposed to the drug alone and in combination with radiation at different pH of the cell culture media. The end point was clonogenic ability of the single-plated cells after the treatment. Results: Cytotoxicity and radiosensitization of IB increased with higher drug concentration and longer exposure time. The most significant radiosensitization was seen with IB (1.5 mM) for 2-h treatment at pH 6.7 before irradiation The dose-modifying factor as defined by the ratio of radiation doses required to achieve the same effect on cell survival was 1.8 at 10% survival level. In contrast, SC-236 (50 μM for 2-8 h) showed no pH-dependent cytotoxicity. There was modest increase in the cell killing at lower doses of radiation. Conclusion: An acidic pH was an important factor affecting the increased cytotoxicity and radiosensitization by ibuprofen. Radiation response was enhanced at shoulder portion of the cell survival curve by selective COX-2 inhibitor.

IT **170569-86-5**, SC-236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pronounced radiosensitization of cultured human cancer cells by COX inhibitor under acidic microenvironment)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 47 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

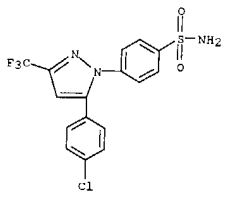
L3 ANSWER 48 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:513730 CAPLUS
DOCUMENT NUMBER: 138:198227
TITLE: Cyclooxygenase inhibition reduces tumor growth and metastasis in an orthotopic model of breast cancer
AUTHOR(S): Connolly, E. M.; Harmey, J. H.; O'Grady, T.; Foley, D.; Roche-Nagle, G.; Kay, E.; Bouchier-Hayes, D. J.
CORPORATE SOURCE: Education and Research Centre, Royal College of Surgeons in Ireland, Department of Surgery, Beaumont Hospital, Dublin, Ire.
SOURCE: British Journal of Cancer (2002), 87(2), 231-237
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of selective and non-selective cyclo-oxygenase inhibition on tumor growth and metastasis in an orthotopic model of breast cancer was investigated. 4T1 mammary adenocarcinoma cells were injected into the mammary fat pad of female BALB/c mice. When tumors reached a mean tumor diameter of 8.4±0.4 mm, mice were randomized into three groups (n=6 per group) and received daily i.p. injections of the selective cyclooxygenase-2 inhibitor, SC-236, the non selective cyclooxygenase inhibitor, Indomethacin, or drug vehicle. Tumor diameter was recorded on alternate days. From 8 days after initiation of treatment, tumor diameter in animals treated with either SC-236 or indomethacin was significantly reduced relative to controls. Both primary tumor weight and the number of lung metastases were significantly reduced in the SC-236 and indomethacin treated mice. Microvessel d. was reduced and tumor cell apoptosis increased in the primary tumor of mice treated with either the selective or non-selective cyclooxygenase inhibitor. In vitro, cyclooxygenase inhibition decreased vascular endothelial growth factor production and increased apoptosis of tumor cells. Our results suggest that cyclooxygenase inhibitors will be of value in the treatment of both primary and metastatic breast cancer.

IT **170569-86-5**, SC-236
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective vs. non-selective COX inhibitors effect on VEGF, apoptosis, tumor growth, angiogenesis, and metastasis in breast adenocarcinoma)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 48 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



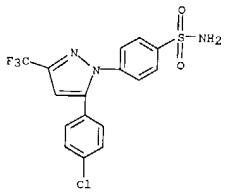
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L3 ANSWER 49 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:435659 CAPLUS
DOCUMENT NUMBER: 138:49502
TITLE: A cyclooxygenase-2 (COX-2) inhibitor compared with dexamethasone in a survival study of rats with intracerebral 9L gliosarcomas
AUTHOR(S): Portnow, Jana; Suleman, Samia; Grossman, Stuart A.; Eller, Susan; Carson, Kathryn
CORPORATE SOURCE: The Johns Hopkins Oncology Center, Baltimore, MD, 21231, USA
SOURCE: Neuro-Oncology (Charlottesville, VA, United States) (2002), 4(1), 22-25
CODEN: NEURJR; ISSN: 1522-8517
PUBLISHER: ScholarOne, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although dexamethasone is very effective for controlling peritumoral cerebral edema, it is associated with distressing side effects that decrease the quality of life for many patients. One potential mechanism to explain the ability of dexamethasone to repair blood-brain barrier dysfunction is through the inhibition of cyclooxygenase-2 (COX-2). The purpose of this study was to determine in a rat brain tumor model whether SC-236, a selective COX-2 inhibitor, is as effective as dexamethasone. Twenty-nine adult male Fischer 344 rats were implanted with intracerebral 9L gliosarcomas and divided into 3 treatment groups. One group (n = 9) served as controls, another (n = 9) was treated with dexamethasone (3 mg/kg p.o. daily), and a 3rd group (n = 11) received SC-236 (3 mg/kg p.o. daily). A survival study was performed. The median survival in the control group was 16 days, compared with 23 days for the dexamethasone group and 23 days for the COX-2 inhibitor group. Kaplan-Meier anal. on pairwise group comparisons showed improved survival that was statistically significant for each treatment group compared with the control group (log-rank), and no significant difference in survival for the COX-2 compared with dexamethasone. These results suggest that a selective COX-2 inhibitor appears to be as effective as dexamethasone in prolonging survival in a rat brain tumor model.

IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(a COX-2 inhibitor (SC-236) compared with dexamethasone in intracerebral 9L gliosarcomas)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 49 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



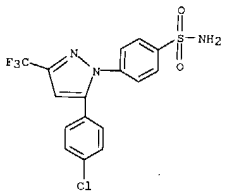
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L3 ANSWER 50 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:405123 CAPLUS
DOCUMENT NUMBER: 138:117388
TITLE: Effects of cyclooxygenase and lipoxygenase inhibition on basal- and serotonin-induced ion transport in rat colon
AUTHOR(S): Engelmann, Bodil Elisabeth; Bindslev, Niels; Poulsen, Steen Seier; Hansen, Mark Berner
CORPORATE SOURCE: The Panum Institute, Department of Medical Physiology, University of Copenhagen, Copenhagen, DK-2200 N, Den.
SOURCE: Comparative Biochemistry and Physiology, Part C: Toxicology & Pharmacology (2002), 132C(1), 37-52
CODEN: CBPPFK; ISSN: 1532-0456
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to determine the effect of a selective cyclooxygenase (COX)-2 inhibitor as compared to non-selective COX and lipoxygenase (LOX) inhibitors in rat colon. Basal- and serotonin (5-hydroxytryptamine, 5-HT)-induced electrogenic ion transport (short circuit current, SCC), prostaglandin E2 (PGE2) release and histol. characteristics were measured. Muscle-stripped mucosal sheets of the proximal and distal segment of rat colon were investigated by employing the Ussing chamber technique, RIAs for PGE2 and light microscopy examns. for control of tissue integrity. 5-HT and PGE2 both induced a concentration-dependent increase in SCC by activation of multiple receptors. The response to 5-HT was bumetanide-sensitive. Neither the non-selective COX inhibitor piroxicam, nor the selective COX-2 inhibitor SC-'236, altered basal- SCC or 5-HT-induced SCC. Indomethacin reduced both basal- and 5-HT-induced SCC in both segments. Nordihydroguaiaretic acid reduced the 5-HT-induced increase in SCC, but did not change basal SCC. 5-HT-induced a concentration-dependent release of PGE2. Only high concns. of piroxicam and indomethacin reduced basal PGE2 release and 5-HT-induced PGE2 release. Histol. examination of the specimens demonstrated only minor changes following mounting in chambers. There were no apparent differences in the morphol. following treatment with COX or LOX inhibitors. These results suggest that in rat colon only the COX-1 enzyme is expressed under basal conditions. Furthermore, data suggest neither the COX-1 nor the COX-2 enzyme to be of major importance for 5-HT-induced ion transport in rat colon in vitro. In conclusion, this study supports 5-HT as a mediator of chloride secretion by activating several receptor subtypes and the LOX enzyme, releasing mediators such as leukotrienes.

IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); BIOL (Biological study)
(effects of cyclooxygenase and lipoxygenase inhibition on basal- and serotonin-induced ion transport in rat colon)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 50 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



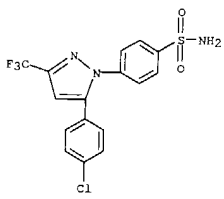
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L3 ANSWER 51 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:366093 CAPLUS
DOCUMENT NUMBER: 137:210569
TITLE: Cyclooxygenase-2, player or spectator in cyclooxygenase-2 inhibitor-induced apoptosis in prostate cancer cells
AUTHOR(S): Song, Xueqin; Lin, Ho-Pi; Johnson, Amy J.; Tseng, Ping-Hui; Yang, Ya-Ting; Kulp, Samuel K.; Chen, Ching-Shih
CORPORATE SOURCE: Division of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, Lexington, USA
SOURCE: Journal of the National Cancer Institute (2002), 94(8), 585-591
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antitumor activity of cyclooxygenase-2 (COX-2) inhibitors is thought to involve COX-2 enzyme inhibition and apoptosis induction, but it is unclear whether COX-2 inhibition is required for apoptosis. Different COX-2 inhibitors have similar IC50 values (concentration for 50% inhibition) for COX-2 inhibition but differ considerably in their abilities to induce apoptosis, suggesting the involvement of a COX-2-independent pathway in apoptosis. To test this hypothesis, we investigated the effect of COX-2 depletion on apoptosis and performed a structure-activity anal. of the COX-2 inhibitor celecoxib in the androgen-independent prostate cancer cell line PC-3. Tetracycline-inducible (Tet-On) COX-2 antisense clones were isolated to assess the effect of COX-2 expression on cell viability and sensitivity to apoptosis induced by COX-2 inhibitors. Untreated Tet-On clones differentially expressed COX-2, and doxycycline-treated clones were depleted of COX-2. We synthesized and characterized various celecoxib derivs. with various COX-2 inhibitory activities and determined their apoptotic activity in PC-3 cells. Apoptosis was assessed with 4 tests. In contrast to the effect of COX-2 inhibitors, which induced apoptosis, COX-2 depletion did not induce cell death. Susceptibility to COX-2 inhibitor-induced apoptosis was independent of the level of COX-2 expression. Structure-activity anal. found no correlation between apoptosis induction and COX-2 inhibition. Some celecoxib derivs. that lacked COX-2 inhibitory activity facilitated apoptosis and vice versa. Moreover, celecoxib and apoptosis-active celecoxib derivs. mediated cell death by inhibiting the same pathway. We have dissociated the apoptosis-inducing activity from the COX-2 inhibitory activity by structural modifications of the COX-2 inhibitor celecoxib. This separation of activities may provide a mol. basis for the development of new classes of apoptosis-inducing agents.

IT **170569-86-5**, 4-[5-(4-Chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(celecoxib derivs. ax COX-2 inhibitors and apoptosis inducers in

L3 ANSWER 51 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
prostate cancer cells)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



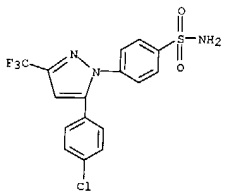
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 52 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:305400 CAPLUS
DOCUMENT NUMBER: 137:273079
TITLE: Epidural injection of cyclooxygenase-2 inhibitor attenuates pain-related behavior following application of nucleus pulposus to the nerve root in the rat
AUTHOR(S): Kawakami, Mamoru; Matsumoto, Takuji; Hashizume, Hiroshi; Kuribayashi, Koichi; Tamaki, Tetsuya
CORPORATE SOURCE: Department of Orthopaedic Surgery, Wakayama Medical University, Wakayama, 641-0012, Japan
SOURCE: Journal of Orthopaedic Research (2002), 20(2), 376-381
CODEN: JOREDR; ISSN: 0736-0266
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclooxygenase-2 (COX-2), the inducible isoform of COX, has been identified as the key enzyme to regulate prostaglandin E2 synthesis in inflammatory conditions. Although it has been reported that COX-2 is present in herniated disk samples obtained from patients, little is known concerning the relationships between COX-2 and painful radiculopathy. The purpose of this study was to evaluate whether epidural injection of COX-2 inhibitor abolishes hyperalgesia induced by nucleus pulposus, which is a pain-related behavior in the rat. Rats, in which nucleus pulposus was relocated on the nerve root, exhibited evidence of mech. hyperalgesia. Epidural injection of COX-2 inhibitor resulted in decrease in mech. hyperalgesia 1 h, 3 and 7 days after the epidural injection of COX-2 inhibitor (0.1 mg/kg SC-'236 dissolved in the vehicle). There were no significant differences in sensitivity to thermal noxious stimuli after either application of the nucleus pulposus or epidural injections. These results suggest that prostaglandins and thromboxane, which are produced by COX-2 in inflammatory cells, appear to be related to the inflammatory process produced by application of nucleus pulposus to the nerve root. It is possible that COX-2 plays a significant role in painful radiculopathy following herniated nucleus pulposus.

IT **170569-86-5**, Sc-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epidural injection of COX-2 inhibitor attenuates pain-related behavior following application of nucleus pulposus to nerve root in rat)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 52 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 53 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:107158 CAPLUS
DOCUMENT NUMBER: 136:161365
TITLE: Aldosterone antagonist-cyclooxygenase-2 inhibitor combination therapy to prevent or treat inflammation-related cardiovascular disorders
INVENTOR(S): Rocha, Ricardo; Zack, Marc D.; McMahon, Ellen G.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 273 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009759	A2	20020207	WO 2001-US23601	20010726
WO 2002009759	A3	20021128		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1303308	A2	20030423	EP 2001-961746	20010726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003125312	A1	20030703	US 2001-915784	20010726
US 6716829	B2	20040406		
JP 2004505060	T2	20040219	JP 2002-515311	20010726
EP 1453522	A1	20040908	EP 2001-998044	20011213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003191100	A1	20031009	US 2002-243876	20020913

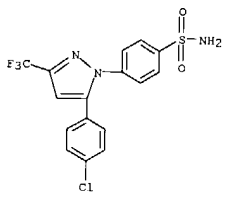
PRIORITY APPLN. INFO.:

US 2000-221364P	P	20000727
US 2001-261497P	P	20010112
US 1999-164390P	P	19991109
US 2000-211064P	P	20000613
US 2000-211250P	P	20000613
US 2000-211253P	P	20000613
US 2000-211264P	P	20000613
US 2000-211311P	P	20000613
US 2000-211340P	P	20000613

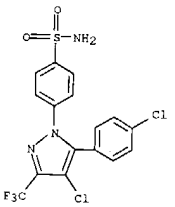
L3 ANSWER 53 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 2000-211451P	P	20000613
US 2000-211459P	P	20000613
US 2000-221358P	P	20000727
US 2000-233056P	P	20000914
US 2000-709253	A2	20001108
US 2000-712543	A1	20001114
US 2001-261352P	P	20010112
WO 2001-US23601	W	20010726
WO 2001-US48419	W	20011213

OTHER SOURCE(S): MARPAT 136:161365
AB Combinations of aldosterone blockers and Cyclooxygenase-2 inhibitors useful in the treatment of inflammation-related cardiovascular disorders are disclosed.
IT **170569-86-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aldosterone antagonist-cyclooxygenase-2 inhibitor combination therapy to prevent or treat inflammation-related cardiovascular disorders)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

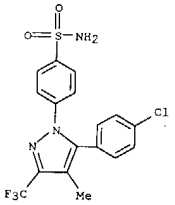


L3 ANSWER 54 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:97650 CAPLUS
DOCUMENT NUMBER: 137:119040
TITLE: Estimation of Binding Affinities for Celecoxib Analogues with COX-2 via Monte Carlo-Extended Linear Response
AUTHOR(S): Wesolowski, Steven S.; Jorgensen, William L.
CORPORATE SOURCE: Department of Chemistry, Yale University, New Haven, CT, 06520-8107, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(3), 267-270
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Monte Carlo (MC)-extended linear response (ELR) calcns. have been used for prediction of binding affinities of celecoxib analogs with the COX-2 enzyme. Three phys. motivated descriptors from the MC simulations were used in a regression equation to fit 45 exptl. activities with R2=0.71 and Q2=0.68. The ELR approach provides a promising screen for optimization of enzyme inhibitors.
IT **170569-50-3 170569-54-7 170569-55-8 170569-86-5 170569-92-3 170569-94-5**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estimation of binding affinities for celecoxib analogs with COX-2 via Monte Carlo -Extended Linear Response)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

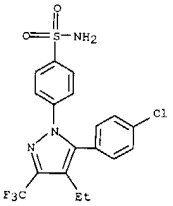


RN 170569-54-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

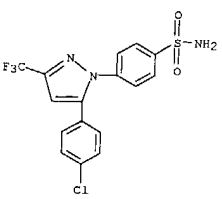
L3 ANSWER 54 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



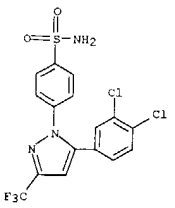
RN 170569-55-8 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-ethyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



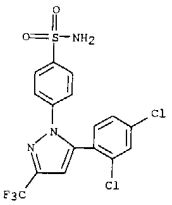
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 54 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 170569-92-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

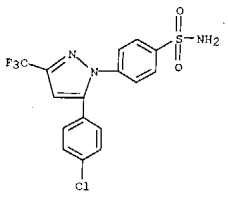


RN 170569-94-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L3 ANSWER 55 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
antiinflammatories)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

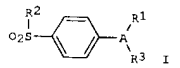


REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L3 ANSWER 55 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:84600 CAPLUS
DOCUMENT NUMBER: 136:151161
TITLE: Preparation of 4-(heterocyclyl)benzenesulfonamides as components of a combination of a cyclooxygenase-2 inhibitors and a leukotriene B4 receptor antagonist
INVENTOR(S): Isakson, Peter C.; Anderson, Gary D.; Gregory, Susan A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 489,415, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6342510	B1	20020129	US 1996-661641	19960611
CA 2224563	AA	19961227	CA 1996-2224563	19960611
US 2002107276	A1	20020808	US 2002-38080	20020103
PRIORITY APPLN. INFO.:			US 1995-489415	B2 19950612
			US 1996-661641	A1 19960611

OTHER SOURCE(S): MARPAT 136:151161
GI



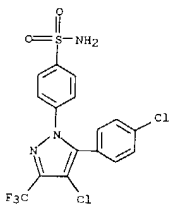
AB The title compds. [I; A = (partially) unsatd. heterocyclyl or carbocyclyl; R1 = (un)substituted heterocyclyl, cycloalkyl, cycloalkenyl, aryl; R2 = Me, NH2; R3 = H, halo, alkyl, etc.] which are cyclooxygenase-2 inhibitors used in combination with a leukotriene B4 receptor antagonists for treatment of inflammation and inflammation-related disorders, were prepared and formulated. Thus, treating Et trifluoroacetate with NaOMe in Me tert-Bu ether followed by addition of 4'-chloroacetophenone (85%), and reacting the resulting 4,4,4-trifluoro-1-(4-chlorophenyl)butane-1,3-dione with 4-sulfonamidophenylhydrazine hydrochloride in EtOH afforded 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide (80%).
IT **170569-86-5P**, 4-[5-(4-Chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-(1H-pyrazol-1-yl)benzenesulfonamides as

L3 ANSWER 56 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:71857 CAPLUS
DOCUMENT NUMBER: 136:139826
TITLE: Selective cyclooxygenase-2 inhibitors and vasomodulator compounds for generalized pain and headache pain
INVENTOR(S): Hassan, Fred; Forbes, James C.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 218 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

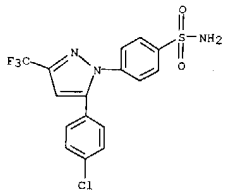
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005799	A2	20020124	WO 2001-US22103	20010713
WO 2002005799	A3	20021121		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002077328	A1	20020620	US 2001-905292	20010713
EP 1299122	A2	20030409	EP 2001-961637	20010713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004503588	T2	20040205	JP 2002-511732	20010713
PRIORITY APPLN. INFO.:			US 2000-218101P P	20000713
			US 2001-284248P P	20010417
			US 2001-296196P P	20010606
			WO 2001-US22103 W	20010713

OTHER SOURCE(S): MARPAT 136:139826
AB A therapeutic combination useful in the treatment, amelioration, prevention, or delay of pain comprising a high energy form of a selective cyclooxygenase-2 inhibitor, a vasomodulator, and a pharmaceutically acceptable excipient, carrier, or diluent, the cyclooxygenase-2 inhibitor and vasomodulator each being present in an amount effective to contribute to the treatment, prevention, or delay of pain. Thus, capsules contained celecoxib 200, Labrasol 280, diethylene glycol monoethyl ether 280, and propylene glycol laurate 140/capsule.
IT **170569-50-3 170569-86-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors and vasomodulators for generalized pain and headache pain treatment)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 56 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



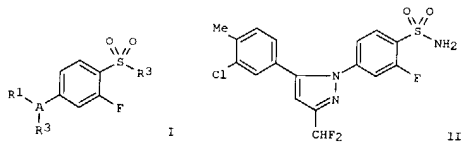
L3 ANSWER 57 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:798213 CAPLUS
DOCUMENT NUMBER: 135:344477
TITLE: Preparation of 2-fluorobenzenesulfonyl-heterocycles with COX-1 and COX-2 inhibiting activity for pharmaceutical use in the treatment of inflammation
INVENTOR(S): Brown, David L.; Graneto, Matthew J.; Ludwig, Cindy L.; Talley, John J.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 242 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081332	A2	20011101	WO 2001-US12983	20010420
WO 2001081332	A3	20020404		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002183362	A1	20021205	US 2001-839424	20010420
EP 1296971	A2	20030402	EP 2001-927279	20010420
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 6600052	B1	20030729	US 2001-838986	20010420
JP 2003531201	T2	20031021	JP 2001-578423	20010420
US 2004092552	A1	20040513	US 2003-258493	20030711
PRIORITY APPLN. INFO.:			US 2000-199533P	P 20000425
			US 2000-253380P	P 20001127
			WO 2001-US12983	W 20010420

OTHER SOURCE(S): MARPAT 135:344477
GI

L3 ANSWER 57 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

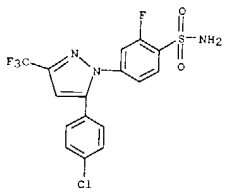


I II

AB 2-Fluorobenzenesulfonyl-heterocycles, such as I [A = 5 or 6 membered heterocycle or carbocycle, such as pyrazole, thiophene, isoxazole, furan; R1 = cyclohexyl, pyridinyl, Ph; R2 = Me, NH2; R3 = H, oxo, CN, halogen, alkyl, alkenyl, carboxyl, haloalkyl, heterocyclyl, cycloalkenyl, aminocarbonyl, etc.] with COX-1 and COX-2 inhibiting activity, were prepared for therapeutic use as anti-inflammatory agents. Thus, pyrazole II was prepared via a multistep synthetic sequence in which the last step was a cyclocondensation reaction of 4-H2NSO2-3-F-C6H3NHNH2 and 3-Cl-4-Me-C6H3COCH2COCHF2 achieved by refluxing for 1 h. concentrated HCl in EtOH to give II with 53% yield. The prepared heterocycles were tested for COX-1 and -2 inhibiting activity.

IT **370874-32-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-fluorobenzenesulfonyl-heterocycles with COX-1 and COX-2 inhibiting activity for pharmaceutical use in the treatment of inflammation)

RN 370874-32-1 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-2-fluoro- (9CI) (CA INDEX NAME)



L3 ANSWER 57 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

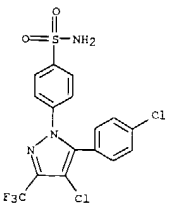
L3 ANSWER 58 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:699248 CAPLUS
DOCUMENT NUMBER: 136:2171
TITLE: QSAR and k-Nearest Neighbor Classification Analysis of Selective Cyclooxygenase-2 Inhibitors Using Topologically-Based Numerical Descriptors
AUTHOR(S): Kauffman, Gregory W.; Jurs, Peter C.
CORPORATE SOURCE: Department of Chemistry, The Pennsylvania State University, University Park, PA, 16802, USA
SOURCE: Journal of Chemical Information and Computer Sciences (2001), 41(6), 1553-1560
CODEN: JCISD8; ISSN: 0095-2338
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Exptl. IC50 data for 314 selective cyclooxygenase-2 (COX-2) inhibitors are used to develop quantitation and classification models as a potential screening mechanism for larger libraries of target compds. Exptl. log(IC50) values ranged from 0.23 to ≥ 5.00. Numerical descriptors encoding solely topol. information are calculated for all structures and are used as inputs for linear regression, computational neural network, and classification anal. routines. Evolutionary optimization algorithms are then used to search the descriptor space for information-rich subsets which minimize the rms error of a diverse training set of compds. An eight-descriptor model was identified as a robust predictor of exptl. log(IC50) values, producing a root-mean-square error of 0.625 log units for an external prediction set of inhibitors which took no part in model development. A k-nearest neighbor classification study of the data set discriminating between active and inactive members produced a nine-descriptor model able to accurately classify 83.3% of the prediction set compds. correctly.

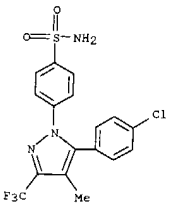
IT **170569-50-3 170569-54-7 170569-55-8 170569-86-5 170569-92-3 170569-94-5**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor; QSAR and k-nearest neighbor classification anal. of selective cyclooxygenase-2 inhibitors using topol.-based numerical descriptors)

RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 58 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

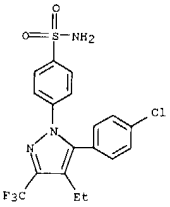


RN 170569-54-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

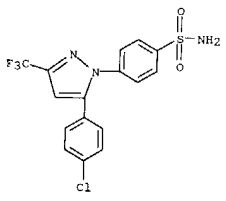


RN 170569-55-8 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-ethyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

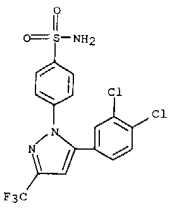
L3 ANSWER 58 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

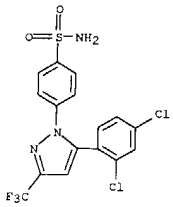


RN 170569-92-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 58 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 170569-94-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

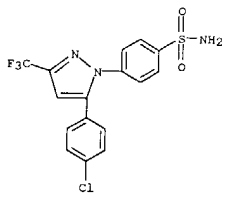
L3 ANSWER 59 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:670121 CAPLUS
DOCUMENT NUMBER: 135:338899
TITLE: COX-2 inhibition as a target in colorectal cancer treatment
AUTHOR(S): Petersen, S.; Eicheler, W.; Petersen, C.; Hunter, N.; Milas, L.
CORPORATE SOURCE: Klinik fur Allgemein- und Abdominalchirurgie, Krankenhaus Dresden-Friedrichstadt, Germany
SOURCE: Chirurgisches Forum fuer Experimentelle und Klinische Forschung (2001) 117-119
CODEN: CFEKA7; ISSN: 0303-6227
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: German

AB Recent studies have suggested that the inhibition of prostaglandin synthesis might have an impact on carcinogenesis in colorectal cancer or that the growth of existing tumors might be inhibited. Especially in gastrointestinal tumors, over-expression of the newly discovered isoform cyclooxygenase 2 (COX-2) was demonstrated. To evaluate the therapeutic option of COX-2 inhibition COX expression was measured in specimens of patients who underwent surgery for colorectal cancer. In addition, a specific COX-2 inhibitor was tested in cell culture and an animal model, using 2 different colorectal cancer cell lines. The transcription of COX-1 and COX-2 was analyzed by RT-PCR in biopsies from colorectal cancer and normal tissue. RNA from shock-frozen samples of 16 patients with colorectal cancer was isolated and the PCR amplicons were analyzed by electrophoresis. In the animal model 2 colorectal cell lines (HT29 and SW620) with different levels of COX-2 expression were grown on the hind leg of nude mice (nu/nu). The selective COX-2 inhibitor SC-236 was given over 10 consecutive days when the tumor was grown to a 6-mm diameter. For angiogenesis studies the so-called skinflap technique was used. The drug was also tested in vitro. According to COX-1 heterogeneous expression was detected in normal tissue and tumor. All of the tumor samples expressed high levels of COX-2. The cell-culture studies revealed a reduction in cell survival after drug treatment in both colorectal cell lines; the effect was more pronounced in HT29. In the animal study the COX-2 inhibitor caused a growth delay of 5.7 days in HT29 cells and 10.3 days in SW620. However, the tumor cell line SW620, with less COX-2 expression, showed a more pronounced effect after treatment with the COX-2 inhibitor. Neoangiogenesis was inhibited by SC-236 in both cell lines, in HT29 28.3 vs 40.4 vessels and in SW620 15.6 vs 22.7 vessels, which was more significant in HT29. RNA transcription for COX-2 was demonstrated in human colorectal cancer specimens. Since there was a lack of COX-2 expression in normal tissue, this might offer a therapeutic gain. The selective COX-2 inhibitor SC-236 had an impact on tumor growth and angiogenesis. However, the inhibiting effect did not correlate with COX-2 expression.

IT **170569-86-5**, SC-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

L3 ANSWER 59 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Uses)
(COX-2 inhibition as a target in colorectal cancer treatment)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



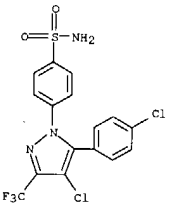
L3 ANSWER 60 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:648842 CAPLUS
DOCUMENT NUMBER: 135:366318
TITLE: Three-Dimensional Quantitative Structure-Activity Relationships of Cyclo-oxygenase-2 (COX-2) Inhibitors: A Comparative Molecular Field Analysis
AUTHOR(S): Chavatte, Philippe; Yous, Saied; Marot, Christophe; Baurin, Nicolas; Lesieur, Daniel
CORPORATE SOURCE: Institut de Chimie Pharmaceutique Albert Lespagnol, Universite de Lille 2, Lille, F-59006, Fr.
SOURCE: Journal of Medicinal Chemistry (2001), 44(20), 3223-3230
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The three-dimensional quant. structure-activity relation (3D-QSAR) approach using comparative mol. field anal. (CoMFA) was applied to an extensive series of 305 varied diarylheterocyclic derivs. known as COX-2 selective inhibitors. X-ray crystal structure of COX-2 bound with SC-558, a selective COX-2 inhibitor, was used to derive the putative bioactive conformation of these inhibitors. Five statistically significant models were obtained from the randomly constituted training sets (229 compds.) and subsequently validated with the corresponding test sets (76 compds.). The best predictive model (n = 229, q2 = 0.714, N = 8, r2 = 0.905, s = 0.291, F = 261.545) was selected for further comparison of the CoMFA contour maps obtained for steric, electrostatic, and lipophilic fields with the enzyme structure. The high level of compatibility with the COX-2 enzyme topol. shows the great accuracy of this model that can predict inhibitory activities for a wide range of compds. and offers important structural insight into designing novel antiinflammatory drugs prior to their synthesis.

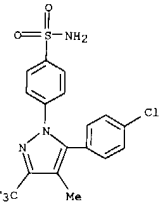
IT **170569-50-3** **170569-54-7** **170569-55-8** **170569-86-5**, Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- **170569-92-3** **170569-94-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(three-dimensional quant. structure-activity relationships of cyclo-oxygenase-2 (COX-2) inhibitors: a comparative mol. field anal.)

RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

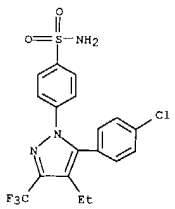
L3 ANSWER 60 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-54-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

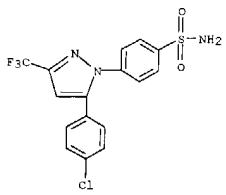


RN 170569-55-8 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-ethyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

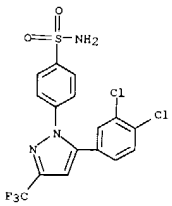


L3 ANSWER 60 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

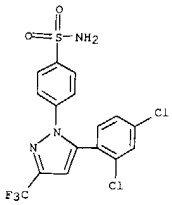


RN 170569-92-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-94-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 60 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

24/09/200410700019

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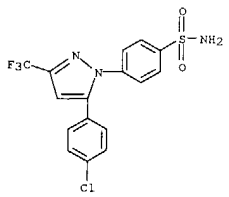
L3 ANSWER 61 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:580990 CAPLUS
DOCUMENT NUMBER: 135:353159
TITLE: Role of transforming growth factor α and prostaglandins in preferential growth of preneoplastic rat hepatocytes
AUTHOR(S): Hufnagl, Karin; Parzefall, Wolfram; Marian, Brigitte; Kafer, Monika; Bukowska, Krystyna; Schulte-Hermann, Rolf; Grasl-Kraupp, Bettina
CORPORATE SOURCE: Institut fur Krebsforschung, University of Vienna, Vienna, A-1090, Austria
SOURCE: Carcinogenesis (2001), 22(8), 1247-1256
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The role of transforming growth factor α (TGFα) and prostaglandins (PGs) in the preferential growth of preneoplastic liver cells was studied. Rats received the genotoxic hepatocarcinogen N-nitrosomorpholine (NNM); placental glutathione S-transferase (GSTp) was used as a marker to identify preneoplastic foci. Preneoplastic foci expressing TGFα (TGFα+) grew more rapidly than TGFα neg. (TGFα-) ones. Almost all tumors studied were pos. for TGFα. The key enzymes of prostaglandin synthesis, cyclooxygenase I (Cox-1) and II (Cox-2), were present in all unaltered and preneoplastic cells and tended to decrease in the later stages of hepatocarcinogenesis. Immunostaining revealed that cultures of hepatocytes, isolated from NNM-treated livers by collagenase perfusion, contained 1-2% GSTp-pos. (GSTp+) and 9% TGFα+ hepatocytes; 0.6% of the cells were GSTp+/TGFα+. Cox-1 and Cox-2 were present in all cells. DNA replication was almost exclusively associated with expression of TGFα. GSTp+ hepatocytes showed a 3- to 4-fold higher probability of TGFα expression and of DNA synthesis than GSTp-neg. (GSTp-) cells. PGE2 or PGF2α increased expression of TGFα and DNA replication in GSTp- cells but not in GSTp+ cells. PGA2 and PGJ2 decreased DNA synthesis in TGFα+ cells without an obvious effect on the intracellular levels of TGFα. The Cox-2 inhibitor SC236 suppressed DNA replication preferentially in GSTp+ cells; this inhibition was reversed by PGE2/F2α. Indomethacin had no effect. These results suggest the following conclusions. (i) Growth regulation of preneoplastic GSTp+ cells in culture exhibits distinct differences from GSTp- cells and elevated expression of TGFα contributes to their growth advantage. (ii) TGFα renders preneoplastic hepatocytes sensitive to suppression of DNA synthesis by PGA2/J2. (iii) SC236, a Cox-2 inhibitor, may have preventive value in hepatocarcinogenesis.

IT **170569-86-5**, SC236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TGF-α and prostaglandins role in preferential growth of preneoplastic rat hepatocytes)

L3 ANSWER 61 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

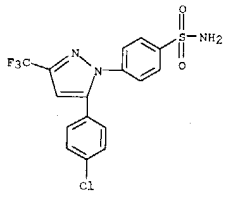
L3 ANSWER 62 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:407626 CAPLUS
DOCUMENT NUMBER: 136:161188
TITLE: Neuroprotection by the selective cyclooxygenase-2 inhibitor SC-236 results in improvements in behavioral deficits induced by reversible spinal cord ischemia
AUTHOR(S): Lapchak, Paul A.; Araujo, Dalia M.; Song, Donhuang; Zivin, Justin A.
CORPORATE SOURCE: Department of Neuroscience, University of California at San Diego, San Diego, CA, 92093-0624, USA
SOURCE: Stroke (2001), 32(5), 1220-1225
CODEN: SJCCA7; ISSN: 0039-2499
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclooxygenase-2 (COX-2), an enzyme that is induced in the central nervous system after various insults, was localized to neurons and in cells associated with the cerebral vasculature, where it may be involved in the inflammatory component of the ischemic cascade. COX-2 is part of the initial reaction that involves the arachidonic acid cascade, which produces mols. that support an inflammatory response. The present study evaluated the pharmacol. effects of a specific long-acting COX-2 inhibitor, SC-236, in a reversible rabbit spinal cord ischemia model using clin. rating scores (behavioral anal.) as the primary end point. SC-236 was administered (10 to 100 mg/kg SC) 5 min after the start of occlusion to groups of rabbits exposed to ischemia induced by temporary (10 to 40 min) occlusion of the intrarenal aorta. Behavioral anal., which allowed for the calcn. of an ET50 value representing the duration of ischemia (minutes) associated with a 50% probability of resultant permanent paraplegia, was conducted 18 and 48 h later. A drug was determined to be neuroprotective if it prolonged the ET50 significantly compared with the appropriate control group. Since SC-236 is not readily soluble in aqueous solns., it was dissolved in 100% DMSO for s.c. administration. Therefore, the vehicle-treated control group consisted of rabbits given an equal volume of DMSO without drug. In the DMSO-treated control group, the ET50 assessed 18 h after initiation of aortal occlusion was 18.84 min. In contrast, treatment with 100 mg/kg of SC-236 given 5 min after the start of occlusion prolonged the ET50 of the group significantly to 30.04, an effect that was still evident 48 h later. In addition, lower doses of the drug (10 and 50 mg/kg) also showed a trend for an increase in ET50. SC-236 (100 mg/kg) did not significantly alter body temperature after a s.c. injection. The present study suggests that COX-2 plays an important role in the ischemic cascade of events that translate into ischemia-induced behavioral deficits and furthermore that selective COX-2 inhibitors may be useful in the treatment of ischemic stroke to improve behavioral functions.

IT **170569-86-5**, SC-236
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2 inhibitor SC-236 is neuroprotective after spinal cord ischemia)

RN 170569-86-5 CAPLUS

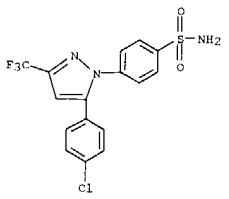
L3 ANSWER 62 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 63 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:125313 CAPLUS
DOCUMENT NUMBER: 134:189362
TITLE: Protective role of cyclooxygenase inhibitors in the adverse action of passive cigarette smoking on the initiation of experimental colitis in rats
AUTHOR(S): Guo, Xin; Liu, Edgar S. L.; Ko, Joshua K. S.; Wong, Benjamin C. Y.; Ye, Yi-Ni; Lam, Shiu-Kum; Cho, Chi-Hin
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, The University of Hong Kong, Hong Kong, Peop. Rep. China
SOURCE: European Journal of Pharmacology (2001), 411(1/2), 193-203
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Clin. and exptl. findings had indicated that cigarette smoke exposure, and cyclooxygenase-2, are strongly associated with inflammatory bowel disease. The role of cyclooxygenase-2 in the pathogenesis of exptl. inflammatory bowel disease as well as in the adverse action of cigarette-smoke exposure was evaluated. Rats were pretreated with different cyclooxygenase-2 inhibitors (indomethacin, nimesulide, or SC-236 (4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide)) along with cigarette-smoke exposure before 2,4,6-trinitrobenzenesulfonic acid-enema. Pretreatment with cyclooxygenase-2 inhibitors not only protected against 2,4,6-trinitrobenzenesulfonic acid-induced inflammatory bowel disease, but also attenuated the potentiating effect of cigarette-smoke exposure on colonic damage. Furthermore, the colonic cyclooxygenase-2 protein and mRNA expression was markedly induced by 2,4,6-trinitrobenzenesulfonic acid-enema, and it was potentiated further by cigarette-smoke exposure, while the cyclooxygenase-1 expression was not changed. Thus, highly induced cyclooxygenase-2 expression not only plays a pathogenic role in 2,4,6-trinitrobenzenesulfonic acid-induced inflammatory bowel disease, but also contributes to the adverse action of cigarette-smoke exposure on this disorder.
IT **170569-86-5**, SC-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(protective role of cyclooxygenase inhibitors in adverse action of passive cigarette smoking on colitis in rats)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

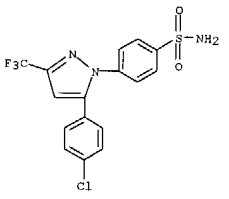
L3 ANSWER 63 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L3 ANSWER 64 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:90367 CAPLUS
DOCUMENT NUMBER: 134:275452
TITLE: Growth inhibition and induction of apoptosis in colorectal tumor cells by cyclooxygenase inhibitors
AUTHOR(S): Richter, M.; Weiss, M.; Weinberger, I.; Furstenberger, G.; Marian, B.
CORPORATE SOURCE: Institute of Cancer Research, University of Vienna, Austria
SOURCE: Carcinogenesis (2001), 22(1), 17-25
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit colorectal carcinogenesis and prevent or revert the growth of premalignant colonic polyps. They inhibit cyclooxygenase (COX) but recent data indicate that this is not the only or even the most important mechanism of inhibition in colorectal tumor cells. We have used colonic carcinoma and adenoma cell lines to study the effects of the NSAID sulindac sulfide, its COX-inactive metabolite, sulindac sulfone, and the isoenzyme-specific inhibitors SC58125, SC236 and SC58560 on tumor cell growth in relation to COX-2 expression and prostaglandin production To establish the role of COX-2 in NSAID action, we constructed clones expressing different levels of COX-2 from SW480 cells. All five compds. inhibited DNA synthesis and/or induced apoptosis, each with a characteristic pattern. ID50s were very similar in all the cell lines and were independent of COX expression, except for the COX-1 inhibitor SC58560, which was least effective in HT29/HI1, the cell line expressing the highest level of COX-1 (ID50 70 μM; in other cell lines the ID50 was 15 μM). For all other compds. ID50 concns. varied less than two-fold: 25-40, 40-90 and 150 μM for SC236, sulindac sulfide and sulindac sulfone, resp. SC58125 was the weakest inhibitor, never causing >50% cell loss. All compds. modulated expression of Bcl-2 and Bak and activated caspase 3. Overexpression of COX-2 in SW480 cells protected them against induction of apoptosis by sulindac sulfide. The effect was restricted to clones producing high levels of prostaglandin E2. In summary, our data indicate that both COX-dependent and COX-independent mechanisms are involved in NSAID-induced growth in colorectal tumor cells. The concns. necessary to inhibit growth were higher than serum concns. that can be obtained in vivo, indicating that the therapeutic effect of NSAIDs cannot be explained by a direct effect of NSAIDs on the epithelial cells alone. For therapeutic purposes, compds. using different targets could be used to minimize side effects while optimizing therapeutic effect.
IT **170569-86-5**, SC 236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(growth inhibition and induction of apoptosis in colorectal tumor cells by cyclooxygenase inhibitors)

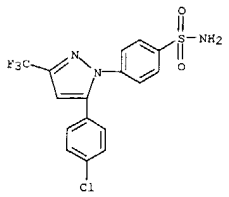
L3 ANSWER 64 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L3 ANSWER 65 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:82714 CAPLUS
DOCUMENT NUMBER: 135:102421
TITLE: Cyclooxygenase-2 inhibitor SC-236 attenuates mechanical allodynia following nerve root injury in rats
AUTHOR(S): DeLeo, Joyce A.; Hashizume, Hiroshi; Rutkowski, Maria D.; Weinstein, James N.
CORPORATE SOURCE: Department of Anesthesiology, Dartmouth-Hitchcock Medical Center, Lebanon, NH, 03756-0001, USA
SOURCE: Journal of Orthopaedic Research (2000), 18(6), 977-982
CODEN: JOREDR; ISSN: 0736-0266
PUBLISHER: Journal of Bone and Joint Surgery, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Low back pain is a common problem, affecting approx. two-thirds of the adult population. Of these individuals, a significant percentage will exhibit symptoms of radicular pain or sciatica. The purpose of this study was to determine the effect of one systemic (2 mg/kg) or intrathecal (0.2 mg/kg) dose of a selective cyclooxygenase-2 inhibitor (SC-236) in decreasing existing mech. allodynia in a rat model of radiculopathy. Gait disturbance and mech. allodynia (increased response to non-noxious von Frey monofilament stimuli) were assessed daily until the rats were killed 7 days after surgery. Robust mech. allodynia developed in the rats in all groups except for those in the sham group by day 1 after surgery. Mech. allodynia was significantly lower in the rats that received the systemic or the intrathecal dose of SC-236 than in those in the vehicle control group (anal. of variance followed by Bonferroni multiple comparison test, $p = 0.002$). The intrathecal drug route of administration produced greater attenuation in allodynia than the systemic dose, supporting a central mechanism of action of the cyclooxygenase-2 inhibitor ($p = 0.002$). The hypothesis that cyclooxygenase-2 is involved in spinal nociceptive processing after a nerve root injury was supported by this study. In addition, these data support continued basic science research to further elucidate central inflammatory processes that follow nerve root injury.
IT **170569-86-5**, SC-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cyclooxygenase-2 inhibitor SC-236 attenuates mech. allodynia following nerve root injury in rats)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 65 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

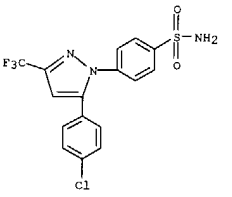
L3 ANSWER 66 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:12289 CAPLUS
DOCUMENT NUMBER: 134:80816
TITLE: Combination of tumors necrosis factor (TNF) antagonists and cyclooxygenase 2 (COX-2) inhibitors for the treatment of inflammation
INVENTOR(S): Keane, J. Timothy
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000229	A1	20010104	WO 2000-US16292	20000626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1189628	A1	20020327	EP 2000-944668	20000626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003503360	T2	20030128	JP 2001-505937	20000626
NZ 515711	A	20040130	NZ 2000-515711	20000626
ZA 2001010349	A	20021218	ZA 2001-10349	20011218

PRIORITY APPLN. INFO.: US 1999-141238P P 19990624
WO 2000-US16292 W 20000626

OTHER SOURCE(S): MARPAT 134:80816
AB The invention provides combinations of a TNF antagonizing agent and a COX-2 inhibiting agent for treating inflammatory disease in a mammal.
IT **170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(TNF antagonist-COX-2 inhibitor combination for inflammation treatment)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 66 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

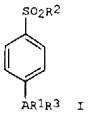


REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 67 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:754502 CAPLUS
DOCUMENT NUMBER: 133:321880
TITLE: Treatment of inflammation and inflammation-related disorders with a combination of a cyclooxygenase-2 inhibitor and a 5-lipoxygenase inhibitor.
INVENTOR(S): Isakson, Peter C.; Anderson, Gary D.; Gregory, Susan A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 489,472, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6136839	A	20001024	US 1996-661660	19960611
CA 2224517	AA	19961227	CA 1996-2224517	19960611
PRIORITY APPLN. INFO.:			US 1995-489472	B2 19950612

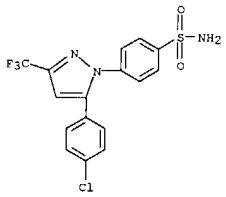
OTHER SOURCE(S): MARPAT 133:321880
GI



I

AB A combination comprising a 5-lipoxygenase inhibitor and a cyclooxygenase-2 inhibitor selected from title compds. [I; A = pyrazolyl; R1 = ≥1 of (substituted) heterocyclyl, cycloalkyl, cycloalkenyl, aryl; R2 = Me, amino; R3 = H, halo, alkyl, alkenyl, alkynyl, oxo, cyano, CO2H, cyanoalkyl, heterocyclyloxy, alkoxy, alkylthio, alkylcarbonyl, aryl, haloalkyl, etc.], is claimed. Thus, EtO2CCHF2 in MeOCMe3 was treated with NaOMe and then with 3-fluoro-4-methoxyacetophenone (preparation given) followed by 16 h stirring to give 96% 4,4-difluoro-1-(3-fluoro-4-methoxyphenyl)butane-1,3-dione. This was refluxed 16 h with 4-sulfonamidophenylhydrazine hydrochloride in EtOH to give 87% 4-[5-(3-fluoro-4-methoxyphenyl)-3-difluoromethyl-1H-pyrazol-1-yl]benzenesulfonamide (II). II with 6-[[3-fluoro-5-(3,4,5,6-tetrahydro-4-methoxy-2H-pyran-4-yl)phenoxy]methyl]-1-methyl-1H-quinazolin-2-one (III) at 30 mpk/day orally in mice in the collagen-induced arthritis screen

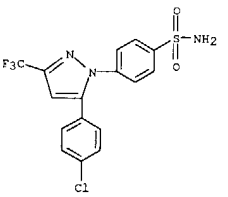
L3 ANSWER 67 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
reduced incidence of arthritis to 20% (vs. 100% for controls). A formulation contg. II and III is given.
IT **170569-86-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of inflammation and inflammation-related disorders with a combination of a cyclooxygenase-2 inhibitor and a 5-lipoxygenase inhibitor)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 68 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:739031 CAPLUS
DOCUMENT NUMBER: 134:261030
TITLE: Discovery of selective COX-2 inhibitors
AUTHOR(S): Talley, John J.; Bertenshaw, Stephen R.; Carter, Jeffery S.; Collins, Paul W.; Docter, Stephen; Graneto, Matthew J.; Isakson, Peter C.; Lee, Len F.; Malecha, James W.; Miyashiro, Julie M.; Penning, Thomas D.; Rogers, Roland S.; Rogier, D. J.; Yu, Stella S.; Anderson, Gary D.; Burton, Earl G.; Cogburn, J. Nita; Gregory, Susan A.; Koboldt, Carol M.; Perkins, William E.; Seibert, Karen; Veenhuizen, Amy W.; Zhang, Yan Y.
CORPORATE SOURCE: Dep. Chemistry, Inflammatory Diseases Research, and Molecular Pharmacology, Chesterfield, MO, 63198, USA
SOURCE: Actualites de Chimie Therapeutique (1999), 25, 123-134
CODEN: ACHTD9; ISSN: 0338-8999
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The results with selective COX-2 inhibitors in laboratory animals and in humans have demonstrated that these mols. are anti-inflammatory, do not inhibit platelet function, and are gastric sparing. A wide variety of 1,2-diarylheterocycles and 1,2-diarylcarbocycles with a para-methylsulfonyl or para-sulfonamide group possess selective inhibitory activity against human cyclooxygenase-2. In particular, 1,5-diarylpyrazole sulfonamides possess exceptional anti-inflammatory activity. Celecoxib has proven to be an excellent anti-inflammatory agent in humans.
IT **170569-86-5P**, Sc-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(diarylheterocycles and diarylcarbocycles with para-methylsulfonyl or para-sulfonamide group as selective COX-2 inhibitors)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

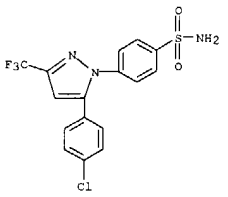
L3 ANSWER 68 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

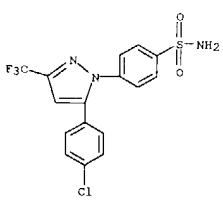
L3 ANSWER 69 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:646368 CAPLUS
DOCUMENT NUMBER: 133:329130
TITLE: Analysis of binding affinities for celecoxib analogues with COX-1 and COX-2 from combined docking and Monte Carlo simulations and insight into the COX-2/COX-1 selectivity
AUTHOR(S): Price, Melissa L. Plount; Jorgensen, William L.
CORPORATE SOURCE: Department of Chemistry, Yale University, New Haven, CT, 06520-8107, USA
SOURCE: Journal of the American Chemical Society (2000), 122(39), 9455-9466
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The origins of binding affinity and COX-2/COX-1 selectivity for analogs of celecoxib have been explored using an approach that combines docking with Monte Carlo (MC) simulations. These inhibitors are COX-2-selective nonsteroidal antiinflammatory drugs (NSAIDs) that are of current interest because the gastrointestinal irritation they cause is reduced compared to that caused by traditional NSAIDs. We report a novel docking method, based on a combined Tabu and Monte Carlo protocol, that dets. starting conformations for MC simulations. Using the docking-predicted starting conformations, relative changes in binding free energies were computed for Me, Et, hydroxymethyl, hydroxyl, thiomethyl, methoxy, trifluoromethyl, chloro, fluoro, and unsubstituted derivs. with the MC free energy perturbation (FEP) method. The computed free energies are in good accord with IC50 values, and the structural information from the simulations can be used to explain the exptl. observed binding trends. In addition, the docking and FEP results have provided clarification of the binding conformation of the phenylsulfonamide moiety and the origin of COX-2/COX-1 selectivity. Namely, the COX- 2 Val → COX-1 Ile substitution is accompanied by an unfavorable conformational shift of the phenylsulfonamide ring.
IT **170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(structure activity relationships of cyclooxygenase-inhibiting celecoxib analogs using combined docking and Monte Carlo simulations)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 69 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



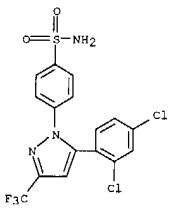
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 70 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:512989 CAPLUS
DOCUMENT NUMBER: 134:25105
TITLE: Three-dimensional quantitative structural activity relationship (3D-QSAR) studies of some 1,5-diarylpyrazoles: Analogue based design of selective cyclooxygenase-2 inhibitors
AUTHOR(S): Desiraju, Gautam R.; Gopalakrishnan, Bulusu; Jetti, Ram K. R.; Raveendra, Dayam; Sarma, Jagarlapudi A. R. P.; Subramanya, Hosahalli S.
CORPORATE SOURCE: School of Chemistry, University of Hyderabad, Hyderabad, 500 046, India
SOURCE: Molecules [online computer file] (2000), 5(7), 945-955
CODEN: MOLEFW; ISSN: 1420-3049
URL: http://www.mdpi.org/molecules/papers/50700945.pdf
PUBLISHER: Molecular Diversity Preservation International
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Selective cyclooxygenase inhibitors have attracted much attention in recent times in the design of new non-steroidal anti-inflammatory drugs (NSAID). 3D-QSAR studies have been performed on a series of 1,5-diarylpyrazoles that act as selective cyclooxygenase-2 (COX-2) inhibitors, using three different methods: comparative mol. field anal. (CoMFA) with partial least squares (PLS) fit; mol. field anal. (MFA) and; receptor surface anal. (RSA) with genetic function algorithms (GFA). The analyses were carried out on 30 analogs of which 25 were used in the training set and the rest considered for the test set. These studies produced reasonably good predictive models with high cross-validated and conventional r2 values in all the three cases.
IT **170569-86-5 170569-94-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(3D-QSAR studies of some 1,5-diarylpyrazoles: design of selective cyclooxygenase-2 inhibitors)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-94-5 CAPLUS

L3 ANSWER 70 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 71 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN

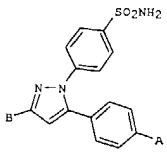
ACCESSION NUMBER: 2000:493525 CAPLUS
DOCUMENT NUMBER: 133:105034
TITLE: Synthesis of 4-[(5-substituted or unsubstituted phenyl)-3-substituted -1H-pyrazol-1-yl]benzenesulfonamides
INVENTOR(S): O'Shea, Paul; Tillyer, Richard D.; Wang, Xin; Clas, Sophie-Dorothee; Dalton, Chad
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042021	A1	20000720	WO 2000-CA34	20000113
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2360354	AA	20000720	CA 2000-2360354	20000113
EP 1144383	A1	20011017	EP 2000-900470	20000113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002534509	T2	20021015	JP 2000-593589	20000113
AU 760888	B2	20030522	AU 2000-30285	20000113
US 6150534	A	20001121	US 2000-483564	20000114
US 6232472	B1	20010515	US 2000-660685	20000913

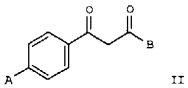
PRIORITY APPLN. INFO.: US 1999-115834P P 19990114
WO 2000-CA34 W 20000113
US 2000-483564 A3 20000114

OTHER SOURCE(S): MARPAT 133:105034
GI

L3 ANSWER 71 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I



II

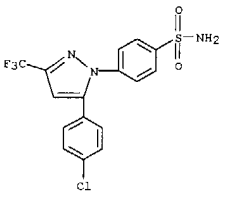
AB The title compds. [I; A = H, halo, Me; B = Me, CH2F, CHF2, CF3] and their solvates, useful as non-steroidal anti-inflammatory agents (no data), were prepared by reacting the butanedione II with 4-sulfonamidophenylhydrazine or its salt or hydrate in an amide solvent at a controlled temperature

IT **284035-41-2P 284035-42-3P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of 4-[(5-substituted or unsubstituted phenyl)-3-substituted -1H-pyrazol-1-yl]benzenesulfonamides)

RN 284035-41-2 CAPLUS
CN Acetamide, N,N-dimethyl-, compd. with 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 170569-86-5
CMF C16 H11 Cl F3 N3 O2 S



CM 2

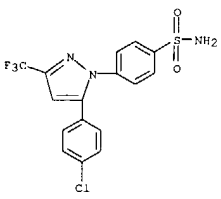
L3 ANSWER 71 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CRN 127-19-5
CMF C4 H9 N O

RN 284035-42-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-, compd. with N,N-dimethylformamide (1:1) (9CI) (CA INDEX NAME)

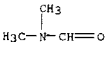
CM 1

CRN 170569-86-5
CMF C16 H11 Cl F3 N3 O2 S



CM 2

CRN 68-12-2
CMF C3 H7 N O



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 72 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN

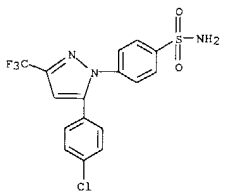
ACCESSION NUMBER: 2000:468528 CAPLUS
DOCUMENT NUMBER: 133:159746
TITLE: Inhibition of cyclooxygenase-2 prevents inflammation-mediated preterm labor in the mouse
AUTHOR(S): Gross, Gil; Imamura, Takuji; Vogt, Sherri K.; Wozniak, David F.; Nelson, D. Michael; Sadovsky, Yoel; Muglia, Louis J.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: American Journal of Physiology (2000), 278(6, Pt. 2), R1415-R1423
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prostaglandins (PGs) have proven important during parturition, but inhibition of PG production treating preterm labor (PTL) results in significant maternal and fetal side effects. We hypothesize that specific inhibition of either cyclooxygenase (COX)-1 or -2 may result in separation of therapeutic and toxic effects. We demonstrate that COX-2, but not COX-1, is induced during inflammation-mediated PTL caused by lipopolysaccharide (LPS) administration. A two- to threefold increase in uterine and ovarian PG concns. coincides with this induction of COX-2. The COX-2-selective inhibitor SC-236 proved effective in stopping preterm delivery and the increases in PGs. The COX-1-selective inhibitor SC-560 also attenuated uterine and ovarian PG production after LPS but did not inhibit PTL as efficiently as SC-236. COX-1-deficient mice, which show delay in the onset of term labor, exhibited no delay in onset of PTL after LPS. These findings suggest that the mechanisms for initiation of inflammation-mediated PTL and term labor differ and that selective COX-2 inhibition may provide a means of stopping inflammation-induced PTL in humans.

IT **170569-86-5**, SC-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cyclooxygenase-2 inhibition prevents inflammation-mediated preterm labor)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 72 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



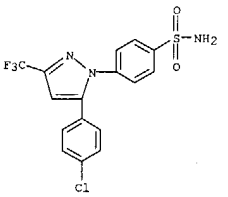
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 73 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:456950 CAPLUS
DOCUMENT NUMBER: 133:84244
TITLE: Method of using a cyclooxygenase-2 inhibitor and an integrin antagonist as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 348 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038786	A2	20000706	WO 1999-US30692	19991222
WO 2000038786	A3	20010308		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356302	AA	20000706	CA 1999-2356302	19991222
EP 1140179	A2	20011010	EP 1999-966594	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102499	T2	20011221	TR 2001-200102499	19991222
JP 2002533422	T2	20021008	JP 2000-590734	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621
PRIORITY APPLN. INFO.:			US 1998-113786P	P 19981223
			WO 1999-US30692	W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor, an integrin antagonist and an antineoplastic agent.
IT **170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES
(Uses)
(cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-

L3 ANSWER 73 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
yl]- (9CI) (CA INDEX NAME)

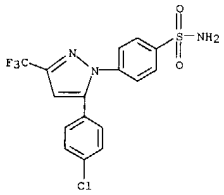


L3 ANSWER 74 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:456927 CAPLUS
DOCUMENT NUMBER: 133:84243
TITLE: Method of using a cyclooxygenase-2 inhibitor and one or more antineoplastic agents as a combination therapy
in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 236 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038730	A2	20000706	WO 1999-US30693	19991222
WO 2000038730	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356606	AA	20000706	CA 1999-2356606	19991222
EP 1140192	A2	20011010	EP 1999-967543	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102499	T2	20011221	TR 2001-200102499	19991222
BR 9916518	A	20020129	BR 1999-16518	19991222
JP 2002533416	T2	20021008	JP 2000-590681	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621
NO 2001003155	A	20010822	NO 2001-3155	20010622
US 2003119895	A1	20030626	US 2002-150546	20020516
US 2003203956	A1	20031030	US 2002-212523	20020805
PRIORITY APPLN. INFO.:			US 1998-113786P	P 19981223
			WO 1999-US30693	W 19991222
			US 2001-857873	A2 20011005

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor and an antineoplastic agent.
IT **170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES
(Uses)
(cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

L3 ANSWER 74 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

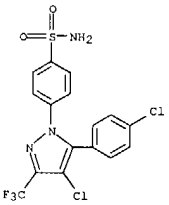


L3 ANSWER 75 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:456913 CAPLUS
DOCUMENT NUMBER: 133:84241
TITLE: Combination therapy of radiation and a cyclooxygenase 2 (COX-2) inhibitor for the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Masferrer, Jaime L.; Milas, Luka
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

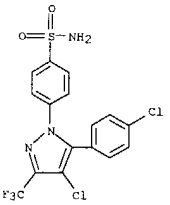
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038716	A1	20000706	WO 1999-US30669	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6649645	B1	20031118	US 1999-385214	19990827
CA 2356547	AA	20000706	CA 1999-2356547	19991222
EP 1140181	A1	20011010	EP 1999-968939	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916544	A	20020108	BR 1999-16544	19991222
JP 2002535249	T2	20021022	JP 2000-590667	19991222
AU 769665	B2	20040129	AU 2000-27134	19991222
NO 2001003064	A	20010823	NO 2001-3064	20010620
US 2004053934	A1	20040318	US 2003-460866	20030613
US 2004053935	A1	20040318	US 2003-461983	20030613
PRIORITY APPLN. INFO.:			US 1998-113786P	P 19981223
			US 1999-385214	A 19990827
			WO 1999-US30669	W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of radiation therapy and a COX-2 inhibitor.
IT **170569-50-3 170569-50-3D**, derivs. **170569-86-5 170569-86-5D**, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(COX-2 inhibitor-radiotherapy combination for neoplasia treatment)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide,
4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-

L3 ANSWER 75 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
pyrazol-1-yl]- (9CI) (CA INDEX NAME)

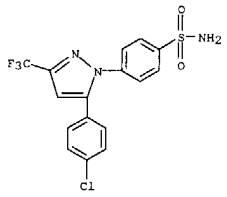


RN 170569-50-3 CAPLUS
CN Benzenesulfonamide,
4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

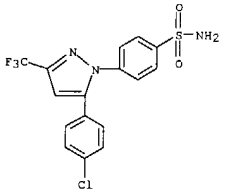


RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 75 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



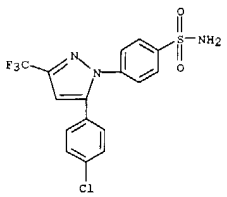
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 76 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:445241 CAPLUS
DOCUMENT NUMBER: 133:331510
TITLE: Enhancement of intrinsic tumor cell radiosensitivity induced by a selective cyclooxygenase-2 inhibitor
AUTHOR(S): Petersen, Cordula; Petersen, Sven; Milas, Luka; Lang, Frederick F.; Tofilon, Philip J.
CORPORATE SOURCE: Departments of Experimental Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Clinical Cancer Research (2000), 6(6), 2513-2520
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antitumor effects of the selective cyclooxygenase (COX)-2 inhibitor SC-236 alone and in combination with radiation were investigated using the human glioma cell line U251 grown in monolayer culture and as tumor xenografts. On the basis of Western and Northern blot analyses, these cells express COX-2 protein and mRNA to levels similar to those in the human colon carcinoma cell line HT29. Treatment of U251 cells in monolayer culture with 50 μM SC-236 resulted in a time-dependent decrease in cell survival as determined by a clonogenic assay. The cell death induced by SC-236 was associated with apoptosis and the detachment of cells from the monolayer. After 2 days of drug treatment, the cells that remained attached were exposed to graded doses of radiation, and the clonogenic assay was performed. Comparison of the survival curves for drug-treated and untreated cultures revealed that SC-236 enhanced radiation-induced cell death. In these combination studies, SC-236 treatment resulted in a dose-enhancement factor of 1.4 at a surviving fraction of 0.1, with the surviving fraction at 2 Gy (SF2) reduced from 0.61 to 0.31. These data indicate that in vitro SC-236 induces U251 apoptotic cell death and enhances the radiosensitivity of the surviving cells. To extend these investigations to an in vivo situation, U251 glioma cells were grown as tumor xenografts in the hind leg of nude mice, and SC-236 was administered in drinking water. SC-236 alone slowed tumor growth rate, and when administered in combination with local irradiation, SC-236 caused a greater than additive increase in tumor growth delay. These in vitro and in vivo results suggest that the selective inhibition of COX-2 combined with radiation has potential as a cancer treatment.

IT **170569-86-5**, SC-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(selective COX-2 inhibitor SC-236 enhancement of intrinsic tumor cell radiosensitivity)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 76 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

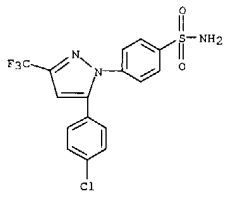
L3 ANSWER 77 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:441655 CAPLUS
DOCUMENT NUMBER: 133:68922
TITLE: Method of using a cyclooxygenase-2 inhibitor and a matrix metalloproteinase inhibitor as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 437 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 21
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037107	A2	20000629	WO 1999-US30776	19991222
WO 2000037107	A3	20010201		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356426	AA	20000629	CA 1999-2356426	19991222
EP 1140194	A2	20011010	EP 1999-968540	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102499	T2	20011221	TR 2001-200102499	19991222
BR 9916536	A	20020102	BR 1999-16536	19991222
JP 2002532563	T2	20021002	JP 2000-589217	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621
NO 2001003156	A	20010823	NO 2001-3156	20010622
PRIORITY APPLN. INFO.:			US 1998-113786P P	19981223
			WO 1999-US30776 W	19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor, a matrix metalloproteinase inhibitor and an antineoplastic agent.

IT **170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 77 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

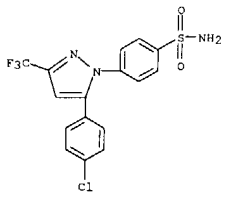


L3 ANSWER 78 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:255160 CAPLUS
DOCUMENT NUMBER: 132:276031
TITLE: Increased radiation sensitivity by the selective COX-2 inhibitor SC-236
AUTHOR(S): Petersen, Cordula; Petersen, Sven; Milas, luka; Tofilon, Philip J.
CORPORATE SOURCE: Klinik und Poliklinik fur Strahlentherapie und Radioonkologie, Medizinische Fakultat Carl Gustav Carus der TU Dresden, Germany
SOURCE: Experimentelle Strahlentherapie und Klinische Strahlenbiologie (2000), 9, 53-56
CODEN: ESKSF9; ISSN: 1432-864X
PUBLISHER: Prof. Dr. Hans-Peter Beck-Bornholdt
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The efficacy of the selective COX-2 inhibitor SC-236 was tested in combination with radiation in vitro and in vivo. Cultures of the human glioblastoma cell line U251 and the murine sarcoma NFSA in rats were used.
After incubation for 2 d, the survival fraction was decreased in the presence of SC-236. The dose-modifying factor at a survival fraction of 0.1 was 1.4. The combination of radiation with SC-236 increased the growth delay from 15 to 63 d. A decrease of TCD50 from 69.2 to 39.2 Gy was achieved in the treatment of NFSA.

IT **170569-86-5**, SC-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(SC-236, COX-2 inhibitor, increased radiation sensitivity of tumors)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

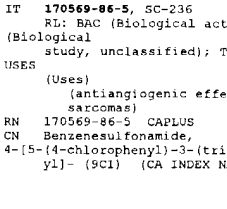
L3 ANSWER 78 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 79 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:255156 CAPLUS
DOCUMENT NUMBER: 132:288428
TITLE: Antiangiogenic effect of selective COX-2 inhibitor SC-'236 by murine sarcomas
AUTHOR(S): Petersen, Sven; Petersen, Cordula; Milas, Luka; Hunter, Nancy R.
CORPORATE SOURCE: Klinik fur Allgemein- und Abdominalchirurgie, Univ. Dresden, Germany
SOURCE: Experimentelle Strahlentherapie und Klinische Strahlenbiologie (2000), 9, 19-21
CODEN: ESKSF9; ISSN: 1432-864X
PUBLISHER: Prof. Dr. Hans-Peter Beck-Bornholdt
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The effect of the selective cyclooxygenase-2 inhibitor SC-'236 (6 mg/kg body weight given orally to mice) on angiogenesis and tumor volume was examined in a murine sarcoma. After 10 days, tumor volume and angiogenesis were reduced.

IT **170569-86-5**, SC-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(antiangiogenic effect of selective COX-2 inhibitor SC-'236 by murine sarcomas)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

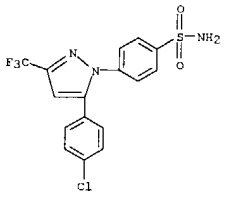
L3 ANSWER 80 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:228872 CAPLUS
DOCUMENT NUMBER: 133:84024
TITLE: Cyclo-oxygenase-2 inhibitors ameliorate the severity of experimental colitis in rats
AUTHOR(S): Karmeli, F.; Cohen, P.; Rachmilewitz, D.
CORPORATE SOURCE: Department of Medicine Hadassah University Hospital, Hebrew University - Hadassah Medical School, Jerusalem, Israel
SOURCE: European Journal of Gastroenterology & Hepatology (2000), 12(2), 223-231
CODEN: EJGHES; ISSN: 0954-691X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Both in exptl. colitis and in inflammatory bowel disease, colonic eicosanoid generation is enhanced and may contribute to the pathogenesis of the inflammatory response. The aim of the study was to evaluate the effect of selective cyclo-oxygenase-2 (COX-2) inhibitors on the extent and severity of two models of exptl. colitis. Colitis was induced by intra-caecal administration of 2 mL 5% acetic acid or intra-colonic administration of 0.1 mL 3% iodoacetamide. Rats were treated intra-gastrically with nimesulide 2 + 10 mg/kg/day, or once with SC-236 6 mg/kg, and killed 1 or 3 days after damage induction. The colon was isolated, weighed, macroscopic damage was measured, and mucosal samples were obtained for histol. and for determination of myeloperoxidase (MPO) and nitric oxide synthase (NOS) activities and eicosanoid generation. The serum levels of thromboxane B2 (TXB2), tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) were determined Nimesulide decreased the extent of colitis induced by acetic acid. Both nimesulide and SC-236 significantly decreased the extent of iodoacetamide-induced colonic damage. The decrease in the extent of colitis induced by nimesulide was accompanied by a significant decrease in mucosal MPO and NOS activities. Nimesulide and SC-236 decreased the enhanced colonic eicosanoid generation in acetic acid and iodoacetamide-induced colitis, and, in iodoacetamide-treated rats, nimesulide also decreased the elevated serum TNF-α and IL-1β levels. The effective nimesulide and SC-236-induced amelioration of the severity of the colitis in acetic acid and iodoacetamide-treated rats confirms the role of eicosanoids in their pathogenesis and suggests that COX-2 inhibitors may be of value in the treatment of inflammatory bowel disease.

IT **170569-86-5**, SC-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cyclo-oxygenase-2 inhibitors ameliorate the severity of exptl. colitis in rats)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

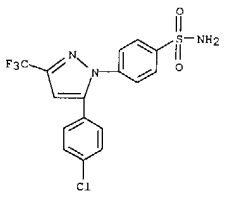
L3 ANSWER 80 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 81 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:199822 CAPLUS
DOCUMENT NUMBER: 132:343696
TITLE: Effective diminution of amniotic prostaglandin production by selective inhibitors of cyclooxygenase type 2
AUTHOR(S): Sadovsky, Yoel; Nelson, D. Michael; Muglia, Louis J.; Gross, Gilad A.; Harris, Katherine C.; Koki, Alane; Masferrer, Jaime L.; Olson, Lisa M.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Washington University School of Medicine, St Louis, MO, USA
SOURCE: American Journal of Obstetrics and Gynecology (2000), 182(2), 370-376
CODEN: AJOGAH; ISSN: 0002-9378
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyclooxygenase inhibitors are effective tocolytic agents, but significant adverse effects limit their use. It was hypothesized that selective inhibitors of the isoenzyme cyclooxygenase 2 would effectively diminish labor-associated prostaglandin production The authors analyzed cyclooxygenase type 1 and 2 expression in amnion, chorion, decidua, and myometrium from laboring or nonlaboring women and tested the efficacy of selective cyclooxygenase 2 inhibition in diminishing prostaglandin production The expression of cyclooxygenase 2 in amnion from women in labor, either preterm or at term, was significantly higher than in amnion before labor. In contrast, cyclooxygenase 1 expression was unchanged by labor. The enhanced expression of amniotic cyclooxygenase 2 was associated with increased prostaglandin E2 levels in laboring women. Amniotic prostaglandin E2 production was effectively diminished by the selective cyclooxygenase 2 inhibitors SC-236 and NS-398 but not by the cyclooxygenase 1 inhibitor SC-560. Selective inhibitors of cyclooxygenase 2 are effective in diminishing prostaglandin production in vitro and may be useful in prevention of preterm deliveries.
IT **170569-86-5**, SC-236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effective diminution of amniotic prostaglandin production by selective inhibitors of cyclooxygenase type 2)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

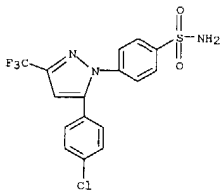
L3 ANSWER 81 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 82 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:191853 CAPLUS
DOCUMENT NUMBER: 132:305254
TITLE: Preferential enhancement of tumor radioresponse by a cyclooxygenase-2 inhibitor
AUTHOR(S): Kishi, Kazushi; Petersen, Sven; Petersen, Cordula; Hunter, Nancy; Mason, Kathryn; Masferrer, Jaime L.; Tofilon, Philip J.; Milas, Luka
CORPORATE SOURCE: Department of Experimental Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Cancer Research (2000), 60(5), 1326-1331
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyclooxygenase-2 (COX-2), an inducible isoform of cyclooxygenase, is overexpressed in many types of malignant tumors, where it mediates production of prostaglandins (PGs), which in turn may stimulate tumor growth and protect against damage by cytotoxic agents. This study investigated whether SC-'236, a selective inhibitor of COX-2, potentiates antitumor efficacy of radiation without increasing radiation injury to normal tissue. Mice bearing the sarcoma FSA in the hind legs were treated daily for 10 days with SC-'236 (6 mg/kg given in the drinking water) when tumors were 6 mm in diameter When tumors reached 8 mm in diameter, the mice were given 11- to 50-Gy single-dose local tumor irradiation with or without SC-'236. SC-'236 inhibited tumor growth on its own, and it greatly enhanced the effect of tumor irradiation The growth delay was increased from 14.8 days after 25-Gy single dose to 28.4 days after the combined treatment (P = 0.01). SC-'236 reduced TCD50 (radiation dose yielding 50% tumor cure) from 39.2 Gy to 20.9 Gy (enhancement factor = 1.87). SC-'236 did not appreciably alter radiation damage to jejunal crypt cells and tissue involved in the development of radiation-induced leg contractures. The SC-'236-induced enhancement of tumor radioresponse was associated with a decrease in PGE2 levels in FSA tumors. The drug had no effect on radiation-induced apoptosis. Neoangiogenesis was inhibited by SC-'236, which could account for some of the increase in tumor radioresponse. Overall, our findings demonstrated that treatment with a selective inhibitor of COX-2 greatly enhanced tumor radioresponse without markedly affecting normal tissue radioresponse. Thus, COX-2 inhibitors have a high potential for increasing the therapeutic ratio of radiotherapy.
IT **170569-86-5**, SC-236
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preferential enhancement of tumor radioresponse by cyclooxygenase-2 inhibitor)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 82 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



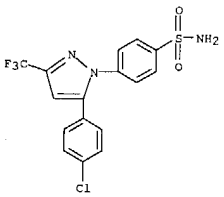
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 83 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:72050 CAPLUS
DOCUMENT NUMBER: 132:342911
TITLE: COX-2 inhibitors: a new class of antiangiogenic agents
AUTHOR(S): Masferrer, Jaime L.; Koki, Alane; Seibert, Karen
CORPORATE SOURCE: Discovery Pharmacology and Analytical Sciences Center,
G.D. Searle/Monsanto Company, St. Louis, MO, 63167, USA
SOURCE: Annals of the New York Academy of Sciences (1999), 889(Cancer Prevention), 84-86
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The role of cyclooxygenase (COX) inhibitors was evaluated in the mouse corneal micropocket assay in which angiogenesis is driven by the addition of a Hydron pellet containing basic fibroblast growth factor (bFGF). Neovascular areas were measured with a slit lamp 5 days after pellet implantation into the corneal stroma. All the animals containing implants with bFGF (90 ng) developed intensive areas of neovascularization. Indomethacin (a nonselective COX-1/COX-2 inhibitor) and SC-236 (a COX-2-selective inhibitor) inhibited angiogenesis in a dose-dependent manner. The indomethacin-treated mice developed severe gastrointestinal toxicity at the ED of 3 mg/kg/day. By contrast, gastrointestinal lesions were not observed, and platelet COX-1 activity was unaffected, at antiangiogenic doses of SC-236 (1-6 mg/kg/day). Furthermore, a COX-1-selective inhibitor, SC-560, was ineffective at doses up to 10 mg/kg, a dose that completely blocked platelet COX-1 activity in these mice. SC-236 was also effective in reducing angiogenesis driven by bFGF, vascular endothelium growth factor, or carrageenan in the matrigel rat model. Finally, in several tumor models, SC-236 consistently and effectively inhibited tumor growth and angiogenesis. This novel antiangiogenic activity of COX-2 inhibitors indicates their potential therapeutic utility in several types of cancer.

IT **170569-86-5**, SC 236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cyclooxygenase-2 inhibitors as antiangiogenic agents)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 83 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 84 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:753114 CAPLUS
DOCUMENT NUMBER: 132:6353
TITLE: Use of a COX-2 inhibitor and a NK-1 receptor antagonist for treating inflammation
INVENTOR(S): Boyce, Susan; Hill, Raymond George; Rupniak, Nadia Melanie
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959635	A1	19991125	WO 1999-GB1632	19990519
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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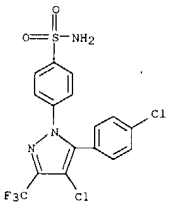
AU 9939486	A1	19991206	AU 1999-39486	19990519
AU 758983	B2	20030403		
EP 1079863	A1	20010307	EP 1999-922393	19990519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002515461	T2	20020528	JP 2000-549299	19990519
US 2004097573	A1	20040520	US 2003-614389	20030707
PRIORITY APPLN. INFO.:			GB 1998-10920 A	19980521
			WO 1999-GB1632 W	19990519
			US 2000-700776 B1	20001120

OTHER SOURCE(S): MARPAT 132:6353

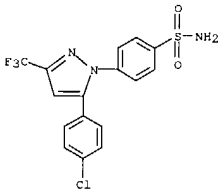
AB The present invention provides the use of a COX-2 inhibitor and a NK-1 receptor antagonist for the manufacture of a medicament for the treatment or prevention of inflammatory disorders, methods of treatment using the COX-2 inhibitor and NK-1 receptor antagonist and pharmaceutical compns. and products containing them. One example NK-1 antagonist is 2R-[1R-[3,5-bis(trifluoromethyl)phenyl]ethoxy]3S-(4-fluorophenyl)-4-(3-(5-oxo-1H,4H-1,2,4-triazolo)methyl]morpholine. Tablet formulations were given.

IT **170569-50-3 170569-86-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2 inhibitor and a NK-1 receptor antagonist for treating inflammation)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 84 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



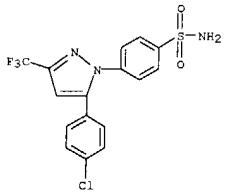
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 85 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 85 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:748317 CAPLUS
DOCUMENT NUMBER: 131:346520
TITLE: Treatment of inflammation and inflammation-related disorders with a combination of a cyclooxygenase-2 inhibitor and a leukotriene A4 hydrolase inhibitor
INVENTOR(S): Isakson, Peter C.; Anderson, Gary D.; Gregory, Susan A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. 5,700,816.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5990148	A	19991123	US 1996-661674	19960611
US 5700816	A	19971223	US 1995-489468	19950612
CA 2224379	AA	19961227	CA 1996-2224379	19960611
PRIORITY APPLN. INFO.:			US 1995-489468	A2 19950612

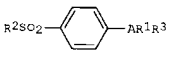
OTHER SOURCE(S): MARPAT 131:346520
AB Combinations of a cyclooxygenase-2 inhibitor and a leukotriene A4 hydrolase inhibitor are described for treatment of inflammation and inflammation-related disorders.
IT **170569-86-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and treatment of inflammation and with a combination of cyclooxygenase-2 and leukotriene A4 hydrolase inhibitors)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 86 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:686709 CAPLUS
DOCUMENT NUMBER: 131:307089
TITLE: Method using cyclooxygenase-2 inhibitors in the treatment and prevention of neoplasia
INVENTOR(S): Seibert, Karen; Masferrer, Jaime; Gordon, Gary B.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5972986	A	19991026	US 1997-949922	19971014
US 2001047024	A1	20011129	US 2001-862128	20010521
US 6469040	B2	20021022		
US 2003220384	A1	20031127	US 2002-226247	20020823
PRIORITY APPLN. INFO.:			US 1997-949922	A1 19971014
			US 1999-390459	B1 19990907
			US 2001-862128	A3 20010521

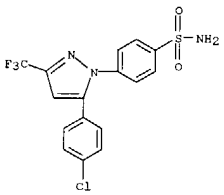
OTHER SOURCE(S): MARPAT 131:307089
GI



I

AB The invention relates to the use of cyclooxygenase-2 inhibitors or derivs.
thereof in preventing and treating neoplasia. In particular, the invention describes the method of preventing and treating epithelial cell neoplasia in a subject, said method comprising treating the subject with a
therapeutically-effective amount of I [A = (partially) unsatd. heterocyclyl,
(partially) unsatd. carbocyclic ring; R1 = (substituted) heterocyclyl, (substituted) cycloalkyl, (substituted) cycloalkenyl, (substituted) aryl; R2 = Me, amino; R3 = H, halo, alkyl, alkenyl, etc.] or a pharmaceutically acceptable salt thereof.
IT **170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cyclooxygenase-2 inhibitors for treatment and prevention of neoplasia)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-

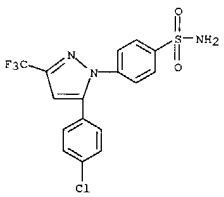
L3 ANSWER 86 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L3 ANSWER 87 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L3 ANSWER 87 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:404851 CAPLUS
DOCUMENT NUMBER: 131:39764
TITLE: Cyclooxygenase-2 inhibitors, alone or with antiviral agents, for treatment of liver disease
INVENTOR(S): Dannenberg, Andrew J.
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930721	A1	19990624	WO 1998-US25206	19981207
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2313049	AA	19990624	CA 1998-2313049	19981207
AU 9917037	A1	19990705	AU 1999-17037	19981207
EP 1039914	A1	20001004	EP 1998-961802	19981207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-69955P P 19971217
WO 1998-US25206 W 19981207

AB Selective inhibitors of cyclooxygenase-2 are used to treat liver disease and in combination with anti-viral drugs to treat virus-caused liver disorders. Selective inhibitors of cyclooxygenase-2 which also inhibit the synthesis of cyclooxygenase-2 improve over the efficacy of conventional selective inhibitors of cyclooxygenase-2 in the treatment of inflammatory conditions, Alzheimer's disease and cancer.

IT **170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cyclooxygenase-2 inhibitors, alone or with antiviral agents, for treatment of liver disease)

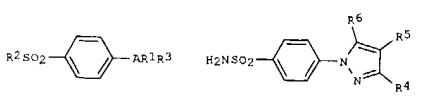
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 88 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:311094 CAPLUS
DOCUMENT NUMBER: 130:347429
TITLE: Method of using cyclooxygenase-2 inhibitors in maintaining the fetal ductus arteriosus during treatment and prevention of preterm labor
INVENTOR(S): Needleman, Philip; Masferrer, Jaime
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9922720	A2	19990514	WO 1998-US22246	19981027
WO 9922720	A3	19990826		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2308639	AA	19990514	CA 1998-2308639	19981027
AU 9911926	A1	19990524	AU 1999-11926	19981027
AU 758566	B2	20030327		
EP 1027048	A2	20000816	EP 1998-955026	19981027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9813164	A	20000822	BR 1998-13164	19981027
JP 2001521889	T2	20011113	JP 2000-518654	19981027
EP 1400242	A1	20040324	EP 2003-27841	19981027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
ZA 9809876	A	19991029	ZA 1998-9876	19981029

PRIORITY APPLN. INFO.: US 1997-63889P P 19971031
EP 1998-955026 A3 19981027
WO 1998-US22246 W 19981027

OTHER SOURCE(S): MARPAT 130:347429
GI



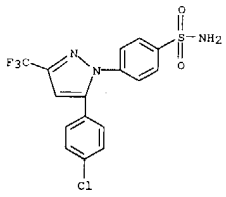
I II

L3 ANSWER 88 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

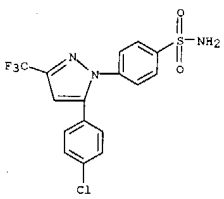
AB Cyclooxygenase-2 (COX-2) inhibitors [I; A = 5- or 6-member ring; R1 = heterocyclo, cycloalkyl, cycloalkenyl, aryl; R2 = alkyl, amino; R3 = halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, alkyloxy, alkylthio, etc.; II; R4 = hydrido, alkyl, haloalkyl, cyano, carboxyl, aminocarbonyl, etc.; R5 = hydrido, alkyl, cyano, cycloalkyl, etc.; R6 = aralkenyl, alkyl, cyano, hydroxyalkyl, cycloalkenyl, heterocyclic) or derivs. thereof are described for maintaining circulation through fetal ductus arteriosus in preventing and treating preterm labor. General synthetic procedures for the active compds. of the present invention are presented. The active compds. may be formulated in various dosage forms. The efficacy of COX-2 inhibitors in preventing closure of the ductus arteriosus is established in a sheep model. A COX-2 inhibitor should be active at a dose of 20 mg/kg.

IT **170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cyclooxygenase-2 inhibitors in maintaining circulation in fetal ductus arteriosus during prevention and treatment of preterm labor)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 89 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 89 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:305133 CAPLUS
DOCUMENT NUMBER: 131:125112
TITLE: Selective inhibition of cyclooxygenase 2 spares renal function and prostaglandin synthesis in cirrhotic rats with ascites
AUTHOR(S): Bosch-Marce, Marta; Claria, Joan; Titos, Esther; Masferrer, Jaime L.; Altuna, Rosario; Poo, Jorge-Luis; Jimenez, Wladimiro; Arroyo, Vicente; Rivera, Francisca; Rodes, Joan
CORPORATE SOURCE: DNA Unit, Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Hospital Clinic, Universitat de Barcelona, Barcelona, Spain
SOURCE: Gastroenterology (1999), 116(5), 1167-1175
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The critical role of cyclooxygenase (COX) products in maintenance of renal function in cirrhosis with ascites discourages the use of nonsteroidal anti-inflammatory drugs in this disease. The recent development of selective COX-2 inhibitors opens new avenues for the use of these compds. in decompensated cirrhosis. The current study evaluates the effects of a selective COX-2 inhibitor (SC-236) on renal function in cirrhotic rats with ascites. In protocol 1, urine volume, urinary excretion of sodium and prostaglandins, glomerular filtration rate, and renal plasma flow were measured before and after administration of SC-236 (n = 12) or ketorolac (n = 10) to rats with cirrhosis. Protocol 2 was aimed at assessing the effects of COX inhibitors on renal water metabolism in 28 cirrhotic rats. Administration of SC-236 to cirrhotic animals did not produce significant renal effects, whereas administration of the nonselective COX-1/COX-2 inhibitor, ketorolac, resulted in a marked reduction in urine volume, urinary excretion of prostaglandins, and glomerular filtration rate and in a significant impairment in renal water metabolism These findings indicate that SC-236 does not significantly impair renal function in rats with cirrhosis.

IT **170569-86-5**, SC 236
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(selective inhibition of cyclooxygenase 2 spares renal function and prostaglandin synthesis in cirrhotic rats with ascites)

RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 90 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:708941 CAPLUS
DOCUMENT NUMBER: 129:339868
TITLE: Method of using cyclooxygenase-2 inhibitors in the prevention of cardiovascular disorders
INVENTOR(S): Roniker, Barbara; LaChapelle, Richard J.; Connolly, Daniel T.; Seibert, Karen; Needleman, Philip
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9847509	A1	19981029	WO 1998-US7318	19980416
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874662	A1	19981113	AU 1998-74662	19980416
AU 745797	B2	20020328		
TR 9902545	T2	20000121	TR 1999-9902545	19980416
EP 979077	A1	20000216	EP 1998-922028	19980416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EE 9900517	A	20000615	EE 1999-517	19980416
BR 9808932	A	20000801	BR 1998-8932	19980416
JP 2001527542	T2	20011225	JP 1998-546113	19980416
EE 200300169	A	20030616	EE 2003-200300169	19980416
ZA 9803249	A	19990419	ZA 1998-3249	19980417
MX 9909495	A	20000930	MX 1999-9495	19991015
NO 9905077	A	19991217	NO 1999-5077	19991018
US 2002035156	A1	20020321	US 2001-946623	20010906
PRIORITY APPLN. INFO.:			US 1997-44626P	P 19970418
			WO 1998-US7318	W 19980416
			US 2000-402634	A1 20000327

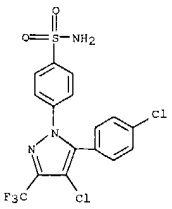
OTHER SOURCE(S): MARPAT 129:339868

AB The invention relates to the use of cyclooxygenase-2 inhibitors or derivs. thereof in preventing cardiovascular disorders.

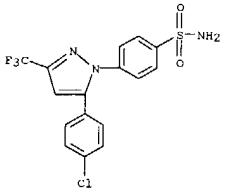
IT **170569-50-3 170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cyclooxygenase-2 inhibitors for prevention of cardiovascular disorders)

RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-

L3 ANSWER 90 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-
yl]- (9CI) (CA INDEX NAME)



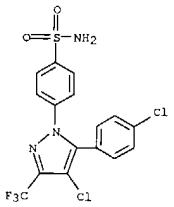
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 91 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:682131 CAPLUS
DOCUMENT NUMBER: 129:286012
TITLE: Method of using cyclooxygenase-2 inhibitors in the treatment and prevention of dementia
INVENTOR(S): Needleman, Philip
PATENT ASSIGNEE(S): G. D. Searle and Co., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

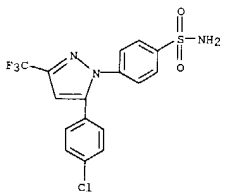
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843648	A1	19981008	WO 1998-US6143	19980330
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9865904	A1	19981022	AU 1998-65904	19980330
AU 725697	B2	20001019		
EP 971714	A1	20000119	EP 1998-912108	19980330
EP 971714	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9807920	A	20000222	BR 1998-7920	19980330
JP 2002514208	T2	20020514	JP 1998-541868	19980330
AT 225660	E	20021015	AT 1998-912108	19980330
ES 2185154	T3	20030416	ES 1998-912108	19980330
ZA 9802808	A	19990406	ZA 1998-2808	19980402
HK 1024872	A1	20030523	HK 2000-104146	20000706
US 2002058688	A1	20020516	US 2001-898772	20010702
PRIORITY APPLN. INFO.:			US 1997-43916P	P 19970403
			WO 1998-US6143	W 19980330
			US 2000-402076	B1 20000113

OTHER SOURCE(S): MARPAT 129:286012
AB The invention relates to the use of cyclooxygenase-2 inhibitors, or derivs. thereof, in preventing and treating dementia. In particular, the invention describes the method of preventing and treating dementia in a subject, said method comprising treating the subject with a therapeutically-effective amount of a pyrazolylbenzenesulfonamide derivative
IT **170569-50-3 170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

L3 ANSWER 91 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Uses)
(cyclooxygenase-2 inhibitors for treatment and prevention of dementia)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide,
4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide,
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



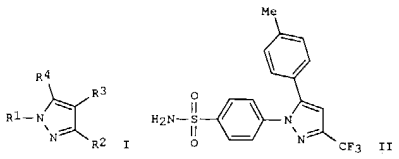
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 92 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:392148 CAPLUS
DOCUMENT NUMBER: 129:54367
TITLE: Substituted pyrazolyl benzenesulfonamides for the treatment of inflammation
INVENTOR(S): Talley, John J.; Penning, Thomas D.; Collins, Paul W.;
Rogier, Donald J., Jr.; Malecha, James W.; Miyashiro, Julie M.; Bertenshaw, Stephen R.; Khanna, Ish K.; Graneto, Matthew J.; Rogers, Roland S.; Carter, Jeffery S.; Docter, Stephen H.; Yu, Stella S.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 55 pp., Cont.-in-part of U. S. 5,521,207.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5760068	A	19980602	US 1996-648113	19960906
US 5466823	A	19951114	US 1993-160594	19931130
US 5521207	A	19960528	US 1994-223629	19940406
WO 9515316	A1	19950608	WO 1994-US12720	19941114
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6156781	A	20001205	US 1999-449076	19991124
US 6413960	B1	20020702	US 2000-609011	20000530
US 6492411	B1	20021210	US 2002-125325	20020417
US 6586603	B1	20030701	US 2002-274679	20021021
US 6716991	B1	20040406	US 2003-378781	20030304
PRIORITY APPLN. INFO.:			US 1993-160594	A2 19931130
			US 1994-223629	A2 19940406
			WO 1994-US12720	W 19941114
			US 1996-648113	A1 19960906
			US 1997-957345	B1 19971024
			US 1999-449076	A1 19991124
			US 2000-609011	A2 20000530
			US 2002-125325	A1 20020417
			US 2002-274679	A1 20021021

OTHER SOURCE(S): MARPAT 129:54367
GI

L3 ANSWER 92 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



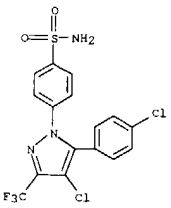
I II

AB A class of pyrazolyl benzenesulfonamide compds. is described for use in treating inflammation and inflammation-related disorders. Several methods of such treatment are claimed, using various subsets of the title compds., e.g., I [R1 = Ph substituted by ≥1 halo, C1-10 alkyl, or sulfamyl; R2 = H, haloalkyl, alkoxycarbonyl, cyano, carboxy, aminocarbonyl, alkylaminocarbonyl, carboxyalkyl, aminocarbonylalkyl, hydroxyalkyl, etc.; R3 = H, alkyl, cyano, alkoxy, hydroxyalkyl, alkylthio, alkylsulfonyl, halo; R4 = (un)substituted aralkenyl, aryl, cycloalkyl, cycloalkenyl, heterocyclyl; with numerous provisos]. Claims also cover use of the compds. in treatment of arthritis, pain, and fever, as well as prevention of colorectal cancer. Over 260 synthetic examples are described. For instance, condensation of 4'-methylacetophenone with Et trifluoroacetate gave 94% yield of crude CF3COCH2COC6H4Me-4. This underwent cyclocondensation with 4-H2NSO2C6H4NHNH2.HCl in refluxing EtOH to give 46% yield of title compound II. The compds. typically showed high selectivity for inhibition of human cyclooxygenase (COX) II over COX I. Selected compds. gave 2-49% inhibition in the carrageenin-induced rat paw edema test at 10-30 mg/kg orally.

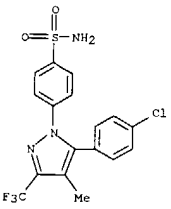
IT **170569-50-3P 170569-54-7P 170569-55-8P**
170569-59-2P 170569-86-5P 170569-92-3P
170569-94-5P 170570-07-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazolylbenzenesulfonamides as antiinflammatories)

RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 92 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

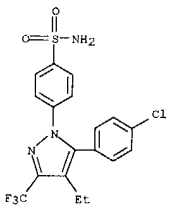


RN 170569-54-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

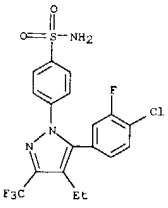


RN 170569-55-8 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-ethyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

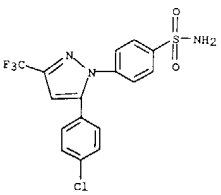
L3 ANSWER 92 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-59-2 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chloro-3-fluorophenyl)-4-ethyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

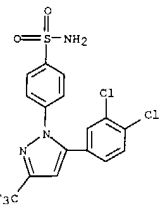


RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

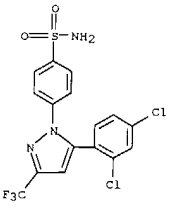


L3 ANSWER 92 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 170569-92-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

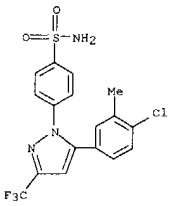


RN 170569-94-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170570-07-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chloro-3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 92 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

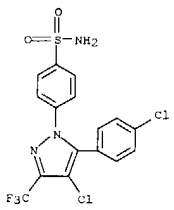
L3 ANSWER 93 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:251054 CAPLUS
DOCUMENT NUMBER: 128:304042
TITLE: Method of using cyclooxygenase-2 inhibitors in the treatment and prevention of neoplasia
INVENTOR(S): Seibert, Karen; Masferrer, Jaime; Gordon, Gary B.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Seibert, Karen; Masferrer, Jaime; Gordon, Gary B.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816227	A1	19980423	WO 1997-US18670	19971014
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2372912	AA	19980423	CA 1997-2372912	19971014
AU 9749048	A1	19980511	AU 1997-49048	19971014
AU 742645	B2	20020110		
EP 932402	A1	19990804	EP 1997-911746	19971014
EP 932402	B1	20040721		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9712314	A	19990831	BR 1997-12314	19971014
JP 2001503395	T2	20010313	JP 1998-518591	19971014
NZ 334921	A	20010330	NZ 1997-334921	19971014
CA 2267186	C	20020514	CA 1997-2267186	19971014
NZ 506515	A	20020531	NZ 1997-506515	19971014
NZ 517374	A	20031031	NZ 1997-517374	19971014
NO 9901793	A	19990415	NO 1999-1793	19990415
NZ 509755	A	20020927	NZ 2001-509755	20010207

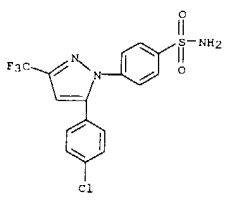
PRIORITY APPLN. INFO.:		
US 1996-28494P	P	19961015
CA 1997-2267186	A3	19971014
WO 1997-US18670	W	19971014
NZ 2001-334921	A1	20010207

OTHER SOURCE(S): MARPAT 128:304042
AB Cyclooxygenase-2 inhibitors or derivs. thereof are used in preventing and treating neoplasia. In particular, the invention describes the method of preventing and treating epithelial cell neoplasia in a subject, said method comprising treating the subject with a therapeutically-effective amount of e.g. p-(R2SO2)PhA(R1)(R3) [A = (partially) unsatd. heterocyclyl,

L3 ANSWER 93 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(partially) unsatd. carbocyclyl; R1 = (substituted) heterocyclyl, (substituted) cycloalk(en)yl, (substituted) aryl; R2 = Me, amino; R3 = H, halo, alkyl, etc.].
IT **170569-50-3 170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(cyclooxygenase-2 inhibitors for treatment and prevention of neoplasia)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

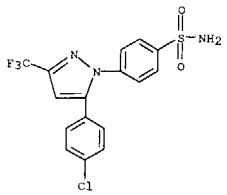
L3 ANSWER 94 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:562996 CAPLUS
DOCUMENT NUMBER: 127:239123
TITLE: Combinations having immunosuppressive effects, containing cyclooxygenase-2-inhibitors and 5-lipoxygenase inhibitors
INVENTOR(S): Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729776	A1	19970821	WO 1997-US1558	19970212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2246265	AA	19970821	CA 1997-2246265	19970212
AU 9718505	A1	19970902	AU 1997-18505	19970212
EP 888127	A1	19990107	EP 1997-904133	19970212
EP 888127	B1	20011212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000504723	T2	20000418	JP 1997-529363	19970212
AT 210461	E	20011215	AT 1997-904133	19970212
PT 888127	T	20020531	PT 1997-904133	19970212
ES 2169351	T3	20020701	ES 1997-904133	19970212
US 6376528	B1	20020423	US 1999-430072	19991018
US 2002143033	A1	20021003	US 2002-98644	20020315

PRIORITY APPLN. INFO.: US 1996-600622 A1 19960213
WO 1997-US1558 W 19970212
US 1998-189463 B1 19981110
US 1999-430072 A3 19991018

OTHER SOURCE(S): MARPAT 127:239123
AB Treatment with a cyclooxygenase-2 inhibitor and a 5-lipoxygenase inhibitor is described as being useful in reducing recipient rejection of transplanted organs and for treatment of autoimmune diseases. 4-[5-(3-Fluoro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide and N'-[3-[5-(4-fluorophenoxy)-2-furyl]-1-methyl-2-propynyl]-N'-hydroxyurea were prepared and a combination of these 2 compds.

L3 ANSWER 94 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
showed a delay in rejection time of skin grafts while treatment alone of each of these compds. resulted in no prolongation of graft survival.
IT **170569-86-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclooxygenase-2 and 5-lipoxygenase inhibitor combinations with immunosuppressive effects)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



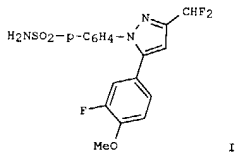
L3 ANSWER 95 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:562995 CAPLUS
DOCUMENT NUMBER: 127:225303
TITLE: Immunosuppressive combinations containing a cyclooxygenase-2 inhibitor and a leukotriene A4 hydrolase inhibitor
INVENTOR(S): Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729774	A1	19970821	WO 1997-US1421	19970211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2246336	AA	19970821	CA 1997-2246336	19970211
AU 9719525	A1	19970902	AU 1997-19525	19970211
EP 880363	A1	19981202	EP 1997-907545	19970211
EP 880363	B1	20020911		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001506574	T2	20010522	JP 1997-529358	19970211
AT 223732	E	20020915	AT 1997-907545	19970211
PT 880363	T	20021231	PT 1997-907545	19970211
ES 2183140	T3	20030316	ES 1997-907545	19970211
US 6407140	B1	20020618	US 2000-489311	20000121
US 2003004191	A1	20030102	US 2002-137231	20020502

PRIORITY APPLN. INFO.: US 1996-600655 A1 19960213
WO 1997-US1421 W 19970211
US 2000-489311 A3 20000121

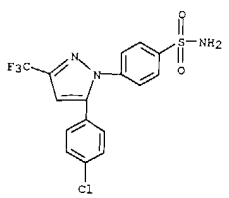
OTHER SOURCE(S): MARPAT 127:225303
GI

L3 ANSWER 95 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

AB Immunosuppressant compns. containing a combination of a cyclooxygenase-2 inhibitor (which inhibits conversion of arachidonic acid to prostaglandins) and a LTA4 hydrolase inhibitor are useful in reducing recipient rejection of transplanted organs and for treatment of autoimmune diseases. Thus, F2CHCO2Et reacted with 3-fluoro-4-methoxyacetophenone to form 4,4-difluoro-1-(3-fluoro-4-methoxyphenyl)butane-1,3-dione, which was condensed with 4-sulfonamidophenylhydrazine-HCl to produce the cyclooxygenase-2 inhibitor I. A formulation was prepared containing 350 mg I and 700 mg 3-[N-methyl-N-[3-[(4-phenylmethyl)phenoxy]propyl]amino]propanoic acid (LTA4 hydrolase inhibitor).
IT **170569-86-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor; immunosuppressive combinations containing cyclooxygenase-2 inhibitor and LTA4 hydrolase inhibitor)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L3 ANSWER 95 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L3 ANSWER 96 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:557660 CAPLUS
DOCUMENT NUMBER: 127:239120
TITLE: Compositions comprising a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist for reducing transplant rejection
INVENTOR(S): Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729775	A1	19970821	WO 1997-US1422	19970211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2246356	AA	19970821	CA 1997-2246356	19970211
AU 9722500	A1	19970902	AU 1997-22500	19970211
EP 880362	A1	19981202	EP 1997-905663	19970211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000505445	T2	20000509	JP 1997-529359	19970211
US 6172096	B1	20010109	US 1998-75633	19980511
US 6617345	B1	20030909	US 2000-659299	20000912
US 2004106668	A1	20040603	US 2003-617222	20030710

PRIORITY APPLN. INFO.:

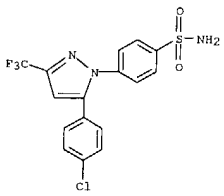
US 1996-600580	A1	19960213
WO 1997-US1422	W	19970211
US 1998-75633	A3	19980511
US 2000-659299	A3	20000912

OTHER SOURCE(S): MARPAT 127:239120

AB Treatment with a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist is described as being useful in reducing recipient rejection of transplanted organs and for treatment of autoimmune diseases.

IT **170569-86-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. comprising a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist for reducing transplant rejection)

L3 ANSWER 96 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



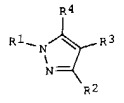
L3 ANSWER 97 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:342369 CAPLUS
DOCUMENT NUMBER: 126:317377
TITLE: Preparation of substituted pyrazolylbenzenesulfonamides for use in veterinary therapies as antiinflammatory agents
INVENTOR(S): Isakson, Peter C.; Talley, John J.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA; Isakson, Peter C.; Talley, John J.
SOURCE: PCT Int. Appl., 214 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9711704	A1	19970403	WO 1996-US15538	19960927
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
US 5756529	A	19980526	US 1995-536318	19950929
CA 2233620	AA	19970403	CA 1996-2233620	19960927
AU 9673768	A1	19970417	AU 1996-73768	19960927
AU 718300	B2	20000413		
EP 854723	A1	19980729	EP 1996-936018	19960927
EP 854723	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1202828	A	19981223	CN 1996-198561	19960927
JP 11514991	T2	19991221	JP 1996-513685	19960927
AT 238058	E	20030515	AT 1996-936018	19960927
IL 123635	A1	20030624	IL 1996-123635	19960927
PT 854723	T	20030829	PT 1996-936018	19960927
ES 2197954	T3	20040116	ES 1996-936018	19960927
NO 9801392	A	19980525	NO 1998-1392	19980327
BR 9610974	A	19990713	BR 1996-10974	19980330

PRIORITY APPLN. INFO.:

US 1995-536318	A1	19950929
WO 1996-US15538	W	19960927

OTHER SOURCE(S): MARPAT 126:317377
GI



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L3 ANSWER 97 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

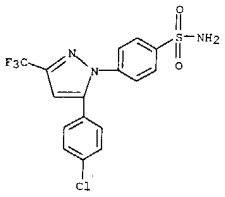
AB The title compds. [I; R1 = substituted aryl (e.g., 4-(H2NSO2)C6H4), heteroaryl; R2 = H, halo, alkyl, etc.; R3 = H, alkyl, halo, etc.; R4 = (un)substituted aralkenyl, aryl, cycloalkyl, etc.], useful in treating inflammation and inflammation-related disorders (e.g., arthritis and pain) in animals, were prepared Thus, reaction of Et trifluoroacetate with 4'-chloroacetophenone in the presence NaOMe in Me tert-Bu ether followed by cyclization of the resulting of 4,4,4-trifluoro-1-(4-chlorophenyl)butane-1,3-dione with 4-sulfonamidophenylhydrazine.HCl in EtOH afforded I [R1 = 4-(H2NSO2)C6H4; R2 = CF3; R3 = H; R4 = 4-ClC6H4] which showed ID50 of <0.1 μM against human cyclooxygenase II.

IT **170569-86-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted pyrazolylbenzenesulfonamides for use in veterinary therapies as antiinflammatory agents)

RN 170569-86-5 CAPLUS

CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



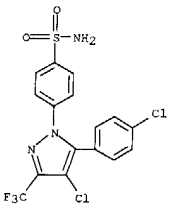
IT **170569-50-3P 170569-54-7P 170569-55-8P 170569-92-3P 170569-94-5P 170570-07-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted pyrazolylbenzenesulfonamides for use in veterinary therapies as antiinflammatory agents)

RN 170569-50-3 CAPLUS

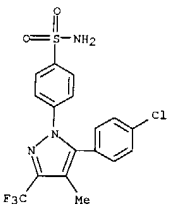
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 97 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-54-7 CAPLUS

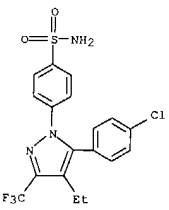
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-55-8 CAPLUS

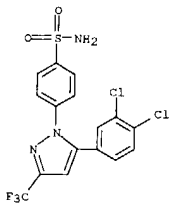
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-ethyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 97 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



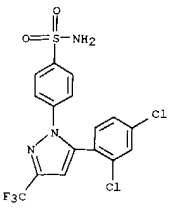
RN 170569-92-3 CAPLUS

CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-94-5 CAPLUS

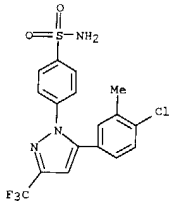
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



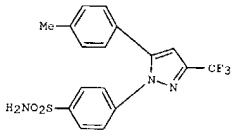
L3 ANSWER 97 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 170570-07-7 CAPLUS

CN Benzenesulfonamide, 4-[5-(4-chloro-3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



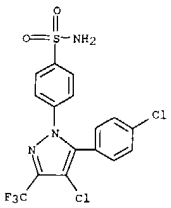
L3 ANSWER 98 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:231026 CAPLUS
DOCUMENT NUMBER: 126:264035
TITLE: Synthesis and Biological Evaluation of the 1,5-Diarylpyrazole Class of Cyclooxygenase-2 Inhibitors: Identification of 4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide (SC-58635, Celecoxib)
AUTHOR(S): Penning, Thomas D.; Talley, John J.; Bertenshaw, Stephen R.; Carter, Jeffery S.; Collins, Paul W.; Docter, Stephen; Graneto, Matthew J.; Lee, Len F.; Malecha, James W.; Miyashiro, Julie M.; Rogers, Roland S.; Rogier, D. J.; Yu, Stella S.; Anderson, Gary D.; Burton, Earl G.; Cogburn, J. Nita; Gregory, Susan A.; Koboldt, Carol M.; Perkins, William E.; Seibert, Karen; Veenhuizen, Amy W.; Zhang, Yan Y.; Isakson, Peter C.
CORPORATE SOURCE: Departments of Chemistry Inflammatory Diseases Research and Molecular Pharmacology, Searle Research and Development, Skokie, IL, 60077, USA
SOURCE: Journal of Medicinal Chemistry (1997), 40(9), 1347-1365
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

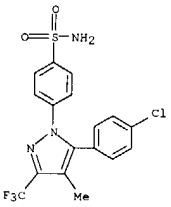
AB Sulfonamide-containing 1,5-diarylpyrazole derivs. were prepared and evaluated for their ability to block cyclooxygenase-2 (COX-2) in vitro and in vivo. Extensive structure-activity relationship work was carried out within this series, and a number of potent and selective inhibitors of COX-2 were identified. Since an early structural lead exhibited an unacceptably long plasma half-life, a number of pyrazole analogs containing potential metabolic sites were evaluated further in vivo in an effort to identify compds. with acceptable pharmacokinetic profiles. This work led to the identification of SC-58635 (celecoxib, I), which is currently in phase III clin. trials for the treatment of rheumatoid arthritis and osteoarthritis.

IT **170569-50-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(diarylpyrazoles as cyclooxygenase 2 inhibitors)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

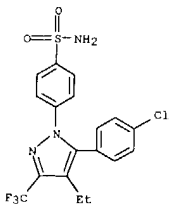


IT **170569-54-7P 170569-55-8P 170569-86-5P 170569-92-3P 170569-94-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(diarylpyrazoles as cyclooxygenase 2 inhibitors)
RN 170569-54-7 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

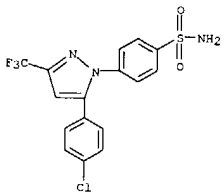
L3 ANSWER 98 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-55-8 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-4-ethyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

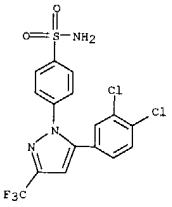


RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

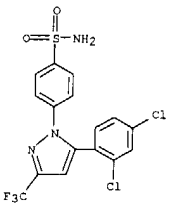


L3 ANSWER 98 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 170569-92-3 CAPLUS
CN Benzenesulfonamide, 4-[5-(3,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 170569-94-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(2,4-dichlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

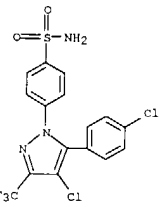


L3 ANSWER 99 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:175052 CAPLUS
DOCUMENT NUMBER: 126:166481
TITLE: Combination of a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist for the treatment of inflammations
INVENTOR(S): Isakson, Peter C.; Anderson, Gary D.; Gregory, Susan A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

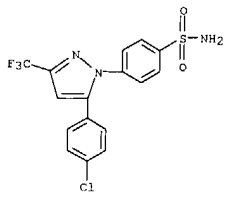
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9641645	A1	19961227	WO 1996-US9905	19960611
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
CA 2224563	AA	19961227	CA 1996-2224563	19960611
AU 9662694	A1	19970109	AU 1996-62694	19960611
EP 833664	A1	19980408	EP 1996-921477	19960611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11507669	T2	19990706	JP 1996-503237	19960611
PRIORITY APPLN. INFO.:			US 1995-489415 A	19950612
			WO 1996-US9905 W	19960611

OTHER SOURCE(S): MARPAT 126:166481
AB Combinations of a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist are described for treatment of inflammation and inflammation-related disorders. The cyclooxygenase-2 inhibitors were prepared. Also, formulations for the drug combination are described.
IT **170569-50-3P 170569-86-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combination of a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist for treatment of inflammation)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 99 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-(5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

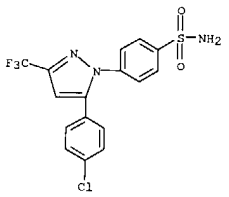


L3 ANSWER 100 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:174993 CAPLUS
DOCUMENT NUMBER: 126:166480
TITLE: Compositions comprising a cyclooxygenase-2 inhibitor and a leukotriene A4 hydrolase inhibitor
INVENTOR(S): Isakson, Peter C.; Anderson, Gary D.; Gregory, Susan A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9641625	A1	19961227	WO 1996-US10105	19960611
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5700816	A	19971223	US 1995-489468	19950612
CA 2224379	AA	19961227	CA 1996-2224379	19960611
AU 9662744	A1	19970109	AU 1996-62744	19960611
EP 843549	A1	19980527	EP 1996-921540	19960611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11507925	T2	19990713	JP 1997-503272	19960611
PRIORITY APPLN. INFO.:			US 1995-489468 A	19950612
			WO 1996-US10105 W	19960611

OTHER SOURCE(S): MARPAT 126:166480
AB Combination of a cyclooxygenase-2 inhibitor and a leukotriene A4 hydrolase inhibitor are described for treatment of inflammation and inflammation-related disorders. Preparation of e.g. 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide is described., as are pharmaceutical formulations and activity against collagen-induced arthritis in mice.
IT **170569-86-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclooxygenase-2 inhibitor and leukotriene A4 hydrolase inhibitor for treatment of inflammation and inflammation-related disorders, compound preparation, pharmaceutical formulations, and antiarthritic activity)
RN 170569-86-5 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

L3 ANSWER 100 OF 103 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **170569-50-3**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor and leukotriene A4 hydrolase inhibitor for treatment of inflammation and inflammation-related disorders, compound preparation, pharmaceutical formulations, and antiarthritic activity)
RN 170569-50-3 CAPLUS
CN Benzenesulfonamide, 4-[4-chloro-5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)